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(54) Title: HUMAN NARCOLEPSY GENE

(57) Abstract: The gene for hypocretin (orexin) receptor 2 (HCRT2), which is associated with narcolepsy, is disclosed. Also described are methods of diagnosis of narcolepsy, pharmaceutical compositions comprising nucleic acids comprising the HCRT2 gene, as well as methods of therapy of narcolepsy.



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## HUMAN NARCOLEPSY GENE

## RELATED APPLICATION

This application is a Continuation-in-Part of U.S. Serial No. 09/426,290, filed October 25, 1999, the entire teachings of which are incorporated herein by  
5 reference.

## BACKGROUND OF THE INVENTION

Narcolepsy, a disorder which affects approximately 1 in 2,000 individuals, is characterized by daytime sleepiness, sleep fragmentation, and symptoms of abnormal rapid eye movement (REM) sleep that include cataplexy (loss of muscle  
10 tone), sleep paralysis, and hypnagogic hallucinations (Aldrich, M.S., *Neurology* 42:34-43 (1992); Siegel, J.M., *Cell* 98:409-412 (1999)). In humans, susceptibility to narcolepsy has been associated with a specific human leukocyte antigen (HLA) alleles, including DQB1\*0602 (Mignot, E., *Neurology* 50:S16-22 (1998); Kadotani, H. *et al.*, *Genome Res.* 8:427-434 (1998); Faraco, J. *et al.*, *J. Hered.* 90:129-132  
15 (1999)); however, attempts to verify narcolepsy as an autoimmune disorder have failed (Mignot, E. *et al.*, *Adv. Neuroimmunol.* 5:23-37 (1995); Mignot, E., *Curr. Opin. Pulm. Med.* 2:482-487 (1996)). In a canine model of narcolepsy, the disorder is transmitted as an autosomal recessive trait, *canarc-1* (Foutz, A.S. *et al.*, *Sleep* 1:413-421 91979); Baker, T.L. and Dement, W.C., *Brain Mechanisms of Sleep* (D.J. McGinty *et al.*, eds., New York: Raven Press, pp. 199-233 (1985)). The possibility  
20 of linkage between *canarc-1* and the canine major histocompatibility complex has been excluded (Mignot, E. *et al.*, *Proc. Natl. Acad. Sci. USA* 88:3475-3478 (1991)).

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A mutation in the hypocretin (orexin) receptor 2 gene in canines has been identified in narcolepsy (Lin, L. *et al.*, *Cell* 98:365-376 (1999)); Hypocrexins/orexins (orexin-A and -B) are neuropeptides associated with regulation of food consumption (de Lecea, L., *et al.*, *Proc. natl. Acad. Sci. USA* 95:322-327 (1998); Sakurai, T. *et al.*, *Cell* 92:573-585 (1998)) as well as other possible functions (Peyron, C. *et al.*, *J. Neurosci.* 18:9996-10015 (1998)). Human cDNA of receptors for orexins have been cloned (Sakurai, T. *et al.*, *Cell* 92:573-585 (1998)), however, full human genes for the orexin receptors have not yet been identified.

Diagnosis of narcolepsy is difficult, as it is necessary to distinguish narcolepsy from other conditions such as chronic fatigue syndrome or other sleep disorders (Ambrogetti, A. and Olson, L.C., *Med. J. Aust.* 160:426-429 (1994); Aldrich, M.S., *Neurology* 50:S2-7 (1998)). Methods of diagnosing narcolepsy based on specific criteria would facilitate identification of the disease, reduce the time and expense associated with diagnosis, and expedite commencement of treatment.

## SUMMARY OF THE INVENTION

As described herein, a full gene for the human hypocretin (orexin) receptor 2 (HCRTR2) has been identified. The sequence of the HCRTR2 gene as described herein is shown in Figure 1 (SEQ ID NO: 1). Accordingly, this invention pertains to an isolated nucleic acid molecule containing the HCRTR2 gene. The invention also relates to DNA constructs comprising the nucleic acid molecules described herein operatively linked to a regulatory sequence, and to recombinant host cells, such as bacterial cells, fungal cells, plant cells, insect cells and mammalian cells, comprising the nucleic acid molecules described herein operatively linked to a regulatory sequence. The invention also pertains to methods of diagnosing narcolepsy in an individual. The methods include detecting the presence of a mutation in the HCRTR2 gene. The invention additionally pertains to pharmaceutical compositions comprising the HCRTR2 nucleic acids of the invention. The invention further pertains to methods of treating narcolepsy, by administering HCRTR2 nucleic acids

of the invention or compositions comprising the HCRTR2 nucleic acids. The methods of the invention allow the accurate diagnosis of narcolepsy and reduce the need for time-consuming and expensive sleep laboratory assessments.

#### BRIEF DESCRIPTION OF THE DRAWINGS

5           Fig. 1A to Fig. 1AY depict the sequence of the human orexin receptor 2 gene (SEQ ID NO:1) and the encoded receptor (SEQ ID NO:2).

The foregoing and other objects, features and advantages of the invention will be apparent from the following more particular description of preferred embodiments of the invention, as illustrated in the accompanying drawings

#### 10   DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a human hypocretin (orexin) receptor 2 (HCRTR2) gene, and the relationship of the gene to narcolepsy. As described herein, Applicants have isolated the HCRTR2 gene. The gene and its products are implicated in the pathogenesis of narcolepsy, as mutations in a closely related  
15   receptor, hypocretin (orexin) receptor 2, have been associated with the presence of narcolepsy in a well-established canine model of narcolepsy (Lin, L. *et al.*, *Cell* 98:365-376 (1999)).

#### NUCLEIC ACIDS OF THE INVENTION

Accordingly, the invention pertains to an isolated nucleic acid molecule  
20   containing the human HCRTR2 gene. The term, "HCRTR2 gene," refers to an isolated genomic nucleic acid molecule that encodes the human hypocretin (orexin) receptor 2. As used herein, the term, "genomic nucleic acid molecule" indicates that the nucleic acid molecule contains introns and exons as are found in genomic DNA (i.e., not cDNA). The nucleic acid molecules can be double-stranded or single-  
25   stranded; single stranded nucleic acid molecules can be either the coding (sense) strand or the non-coding (antisense) strand. The nucleic acid molecule can additionally contain a marker sequence, for example, a nucleotide sequence which encodes a polypeptide, to assist in isolation or purification of the polypeptide. Such



sequences include, but are not limited to, those which encode a glutathione-S-transferase (GST) fusion protein and those which encode a hemagglutinin A (HA) peptide marker from influenza. In a preferred embodiment, the nucleic acid molecule has the sequence shown in the Figure (SEQ ID NO:1).

5           As used herein, an "isolated" or "substantially pure" gene or nucleic acid molecule is intended to mean a gene which is not flanked by nucleotide sequences which normally (in nature) flank the gene (as in other genomic sequences). Thus, an isolated gene can include a gene which is synthesized chemically or by recombinant means. Thus, recombinant DNA contained in a vector are included in the definition  
10 of "isolated" as used herein. Also, isolated nucleotide sequences include recombinant DNA molecules in heterologous host cells, as well as partially or substantially purified DNA molecules in solution. Such isolated nucleotide sequences are useful in the manufacture of the encoded protein, as probes for isolating homologous sequences (e.g., from other mammalian species), for gene  
15 mapping (e.g., by *in situ* hybridization with chromosomes), or for detecting expression of the HCRTR2 gene in tissue (e.g., human tissue), such as by Northern blot analysis.

          The present invention also encompasses variations of the nucleic acid sequences of the invention. Such variations can be naturally-occurring, such as in  
20 the case of allelic variation, or non-naturally-occurring, such as those induced by various mutagens and mutagenic processes. Intended variations include, but are not limited to, addition, deletion and substitution of one or more nucleotides which can result in conservative or non-conservative amino acid changes, including additions and deletions. Preferably, the nucleotide or amino acid variations are silent or  
25 conserved; that is, they do not alter the characteristics or activity of the hypocretin (orexin) receptor 2.

          Other alterations of the nucleic acid molecules of the invention can include, for example, labeling, methylation, internucleotide modifications such as uncharged linkages (e.g., methyl phosphonates, phosphotriesters, phosphoamidates,  
30 carbamates), charged linkages (e.g., phosphorothioates, phosphorodithioates), pendent moieties (e.g., polypeptides), intercalators (e.g., acridine, psoralen),

chelators, alkylators, and modified linkages (e.g., alpha anomeric nucleic acids). Also included are synthetic molecules that mimic nucleic acid molecules in the ability to bind to a designated sequences via hydrogen bonding and other chemical interactions. Such molecules include, for example, those in which peptide linkages  
5 substitute for phosphate linkages in the backbone of the molecule.

The invention also relates to fragments of the isolated nucleic acid molecules described herein. The term "fragment" is intended to encompass a portion of a nucleic acid sequence described herein which is from at least about 25 contiguous nucleotides to at least about 50 contiguous nucleotides or longer in length. One or  
10 more introns can also be present. Such fragments are useful as probes, e.g., for diagnostic methods, as described below and also as primers or probes. Particularly preferred primers and probes selectively hybridize to a nucleic acid molecule containing the HCRTR2 gene described herein.

The invention also pertains to nucleic acid molecules which hybridize under  
15 high stringency hybridization conditions, such as for selective hybridization, to a nucleotide sequence described herein (e.g., nucleic acid molecules which specifically hybridize to a nucleic acid containing the HCRTR2 gene described herein). Hybridization probes are oligonucleotides which bind in a base-specific manner to a complementary strand of nucleic acid. Suitable probes include polypeptide nucleic  
20 acids, as described in (Nielsen *et al.*, *Science* 254, 1497-1500 (1991)).

Such nucleic acid molecules can be detected and/or isolated by specific hybridization (e.g., under high stringency conditions). "Stringency conditions" for hybridization is a term of art which refers to the incubation and wash conditions, e.g., conditions of temperature and buffer concentration, which permit hybridization  
25 of a particular nucleic acid to a second nucleic acid; the first nucleic acid may be perfectly (i.e., 100%) complementary to the second, or the first and second may share some degree of complementarity which is less than perfect (e.g., 60%, 75%, 85%, 95%). For example, certain high stringency conditions can be used which distinguish perfectly complementary nucleic acids from those of less  
30 complementarity.

"High stringency conditions", "moderate stringency conditions" and "low stringency conditions" for nucleic acid hybridizations are explained on pages 2.10.1-2.10.16 and pages 6.3.1-6 in *Current Protocols in Molecular Biology* (Ausubel, F.M. *et al.*, "Current Protocols in Molecular Biology", John Wiley & Sons, (1998)) the teachings of which are hereby incorporated by reference. The exact conditions which determine the stringency of hybridization depend not only on ionic strength (e.g., 0.2XSSC, 0.1XSSC), temperature (e.g., room temperature, 42°C, 68°C) and the concentration of destabilizing agents such as formamide or denaturing agents such as SDS, but also on factors such as the length of the nucleic acid sequence, base composition, percent mismatch between hybridizing sequences and the frequency of occurrence of subsets of that sequence within other non-identical sequences. Thus, high, moderate or low stringency conditions can be determined empirically. By varying hybridization conditions from a level of stringency at which no hybridization occurs to a level at which hybridization is first observed, conditions which will allow a given sequence to hybridize (e.g., selectively) with the most similar sequences in the sample can be determined.

Exemplary conditions are described in Krause, M.H. and S.A. Aaronson, *Methods in Enzymology*, 200:546-556 (1991). Also, in, Ausubel, *et al.*, "Current Protocols in Molecular Biology", John Wiley & Sons, (1998), which describes the determination of washing conditions for moderate or low stringency conditions. Washing is the step in which conditions are usually set so as to determine a minimum level of complementarity of the hybrids. Generally, starting from the lowest temperature at which only homologous hybridization occurs, each °C by which the final wash temperature is reduced (holding SSC concentration constant) allows an increase by 1% in the maximum extent of mismatching among the sequences that hybridize. Generally, doubling the concentration of SSC results in an increase in  $T_m$  of ~17°C. Using these guidelines, the washing temperature can be determined empirically for high, moderate or low stringency, depending on the level of mismatch sought.

For example, a low stringency wash can comprise washing in a solution containing 0.2XSSC/0.1% SDS for 10 min at room temperature; a moderate

stringency wash can comprise washing in a prewarmed solution (42°C) solution containing 0.2XSSC/0.1% SDS for 15 min at 42°C; and a high stringency wash can comprise washing in prewarmed (68°C) solution containing 0.1XSSC/0.1%SDS for 15 min at 68°C. Furthermore, washes can be performed repeatedly or sequentially to  
5 obtain a desired result as known in the art. Equivalent conditions can be determined by varying one or more of the parameters given as an example, as known in the art, while maintaining a similar degree of identity or similarity between the target nucleic acid molecule and the primer or probe used.

Hybridizable nucleic acid molecules are useful as probes and primers, e.g.,  
10 for diagnostic applications, as described below. As used herein, the term "primer" refers to a single-stranded oligonucleotide which acts as a point of initiation of template-directed DNA synthesis under appropriate conditions (*e.g.*, in the presence of four different nucleoside triphosphates and an agent for polymerization, such as, DNA or RNA polymerase or reverse transcriptase) in an appropriate buffer and at a  
15 suitable temperature. The appropriate length of a primer depends on the intended use of the primer, but typically ranges from 15 to 30 nucleotides. Short primer molecules generally require cooler temperatures to form sufficiently stable hybrid complexes with the template. A primer need not reflect the exact sequence of the template, but must be sufficiently complementary to hybridize with a template. The  
20 term "primer site" refers to the area of the target DNA to which a primer hybridizes. The term "primer pair" refers to a set of primers including a 5' (upstream) primer that hybridizes with the 5' end of the DNA sequence to be amplified and a 3' (downstream) primer that hybridizes with the complement of the 3' end of the sequence to be amplified.

25 The invention also pertains to nucleotide sequences which have a substantial identity with the nucleotide sequences described herein; particularly preferred are nucleotide sequences which have at least about 70%, and more preferably at least about 80% identity, and even more preferably at least about 90% identity, with nucleotide sequences described herein. Particularly preferred in this instance are  
30 nucleotide sequences encoding hypocretin (orexin) receptor 2.

To determine the percent identity of two nucleotide sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first nucleotide sequence). The nucleotides at corresponding nucleotide positions are then compared. When a position in the first sequence is  
5 occupied by the same nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % identity = # of identical positions/total # of positions x 100).

10 The determination of percent identity between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin *et al.* (*Proc. Natl. Acad. Sci. USA*, 90:5873-5877 (1993)). Such an algorithm is incorporated into the NBLAST program which can be used to  
15 identify sequences having the desired identity to nucleotide sequences of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.* (*Nucleic Acids Res*, 25:3389-3402 (1997)). When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., NBLAST) can be used. See  
20 <http://www.ncbi.nlm.nih.gov>. In one embodiment, parameters for sequence comparison can be set at W=12. Parameters can also be varied (e.g., W=5 or W=20). The value "W" determines how many continuous nucleotides must be identical for the program to identify two sequences as containing regions of identity.

The invention also provides expression vectors containing a nucleic acid  
25 comprising the HCRTR2 gene, operatively linked to at least one regulatory sequence. Many such vectors are commercially available, and other suitable vectors can be readily prepared by the skilled artisan. "Operatively linked" is intended to mean that the nucleic acid sequence is linked to a regulatory sequence in a manner which allows expression of the nucleic acid sequence. Regulatory sequences are art-  
30 recognized and are selected to produce a hypocretin (orexin) receptor 2. Accordingly, the term "regulatory sequence" includes promoters, enhancers, and

other expression control elements such as those described in Goeddel, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). For example, the native regulatory sequences or regulatory sequences native to the transformed host cell can be employed. It should be understood that the

5 design of the expression vector may depend on such factors as the choice of the host cell to be transformed and/or the receptor desired to be expressed. For instance, the gene of the present invention can be expressed by ligating the gene into a vector suitable for expression in either prokaryotic cells, eukaryotic cells or both (see, for example, Broach, *et al.*, *Experimental Manipulation of Gene Expression*, ed. M.

10 Inouye (Academic Press, 1983) p. 83; *Molecular Cloning: A Laboratory Manual*, 2nd Ed., ed. Sambrook *et al.* (Cold Spring Harbor Laboratory Press, 1989) Chapters 16 and 17). Typically, expression constructs will contain one or more selectable markers, including, but not limited to, the gene that encodes dihydrofolate reductase and the genes that confer resistance to neomycin, tetracycline, ampicillin,

15 chloramphenicol, kanamycin and streptomycin resistance. Vectors can also include, for example, an autonomously replicating sequence (ARS), expression control sequences, ribosome-binding sites, RNA splice sites, polyadenylation sites, transcriptional terminator sequences, secretion signals and mRNA stabilizing sequences.

20 Prokaryotic and eukaryotic host cells transformed by the described vectors are also provided by this invention. For instance, cells which can be transformed with the vectors of the present invention include, but are not limited to, bacterial cells such as *E. coli* (e.g., *E. coli* K12 strains), *Streptomyces*, *Pseudomonas*, *Serratia marcescens* and *Salmonella typhimurium*, insect cells (baculovirus), including

25 *Drosophila*, fungal cells, such as yeast cells, plant cells and mammalian cells, such as thymocytes, Chinese hamster ovary cells (CHO), and COS cells. The host cells can be transformed by the described vectors by various methods (e.g., electroporation, transfection using calcium chloride, rubidium chloride, calcium phosphate, DEAE-dextran, or other substances; microprojectile bombardment;

30 lipofection, infection where the vector is an infectious agent such as a retroviral genome, and other methods), depending on the type of cellular host.

The nucleic acid molecules of the present invention can be produced, for example, by replication in a suitable host cell, as described above. Alternatively, the nucleic acid molecules can also be produced by chemical synthesis.

The nucleotide sequences of the nucleic acid molecules described herein  
5 (e.g., a nucleic acid molecule comprising SEQ ID NO:1) can be amplified by methods known in the art. For example, this can be accomplished by e.g., PCR. *See generally PCR Technology: Principles and Applications for DNA Amplification* (ed. H.A. Erlich, Freeman Press, NY, NY, 1992); *PCR Protocols: A Guide to Methods and Applications* (eds. Innis, *et al.*, Academic Press, San Diego, CA, 1990); Mattila  
10 *et al.*, *Nucleic Acids Res.* 19, 4967 (1991); Eckert *et al.*, *PCR Methods and Applications* 1, 17 (1991); *PCR* (eds. McPherson *et al.*, IRL Press, Oxford); and U.S. Patent 4,683,202.

Other suitable amplification methods include the ligase chain reaction (LCR) (see Wu and Wallace, *Genomics* 4, 560 (1989), Landegren *et al.*, *Science* 241, 1077  
15 (1988), transcription amplification (Kwoh *et al.*, *Proc. Natl. Acad. Sci. USA* 86, 1173 (1989)), and self-sustained sequence replication (Guatelli *et al.*, *Proc. Nat. Acad. Sci. USA*, 87, 1874 (1990)) and nucleic acid based sequence amplification (NASBA). The latter two amplification methods involve isothermal reactions based on isothermal transcription, which produce both single stranded RNA (ssRNA) and  
20 double stranded DNA (dsDNA) as the amplification products in a ratio of about 30 or 100 to 1, respectively.

The amplified DNA can be radiolabeled and used as a probe for screening a library or other suitable vector to identify homologous nucleotide sequences. Corresponding clones can be isolated, DNA can be obtained following *in vivo*  
25 excision, and the cloned insert can be sequenced in either or both orientations by art recognized methods, to identify the correct reading frame encoding a protein of the appropriate molecular weight. For example, the direct analysis of the nucleotide sequence of homologous nucleic acid molecules of the present invention can be accomplished using either the dideoxy chain termination method or the Maxam -  
30 Gilbert method (see Sambrook *et al.*, *Molecular Cloning, A Laboratory Manual* (2nd Ed., CSHP, New York 1989); Zyskind *et al.*, *Recombinant DNA Laboratory*

*Manual*, (Acad. Press, 1988)). Using these or similar methods, the protein(s) and the DNA encoding the protein can be isolated, sequenced and further characterized.

#### METHODS OF DIAGNOSIS

The nucleic acids and the proteins described above can be used to detect, in  
5 an individual, a mutation in the HCRTR2 gene that is associated with narcolepsy. In  
one embodiment of the invention, diagnosis of narcolepsy is made by detecting a  
mutation in the HCRTR2 gene. The mutation can be the insertion or deletion of a  
single nucleotide, or of more than one nucleotide, resulting in a frame shift mutation;  
the change of at least one nucleotide, resulting in a change in the encoded amino  
10 acid; the change of at least one nucleotide, resulting in the generation of a premature  
stop codon; the deletion of several nucleotides, resulting in a deletion of one or more  
amino acids encoded by the nucleotides; the insertion of one or several nucleotides,  
such as by unequal recombination or gene conversion, resulting in an interruption of  
the coding sequence of the gene; duplication of all or a part of the gene;  
15 transposition of all or a part of the gene; or rearrangement of all or a part of the gene.  
More than one such mutation may be present in a single gene. Such sequence  
changes cause a mutation in the receptor encoded by the HCRTR2 gene. For  
example, if the mutation is a frame shift mutation, the frame shift can result in a  
change in the encoded amino acids, and/or can result in the generation of a  
20 premature stop codon, causing generation of a truncated receptor. Alternatively, a  
mutation associated with narcolepsy can be a synonymous mutation in one or more  
nucleotides (i.e., a mutation that does not result in a change in the receptor encoded  
by the HCRTR2 gene, such as a mutation in an intron or an untranslated portion of  
the gene). Such a polymorphism may alter splicing sites, affect the stability or  
25 transport of mRNA, or otherwise affect the transcription or translation of the gene.  
A HCRTR2 gene that has any of the mutations described above is referred to herein  
as a "mutant gene." It is likely that a mutation in the HCRTR2 gene is associated  
with narcolepsy in humans because of the association between a mutation in the  
HCRTR2 gene and narcolepsy in dogs (Lin, L. *et al.*, *Cell* 98:365-376 (1999), the  
30 entire teachings of which are incorporated herein by reference). In a preferred



embodiment, the mutation in the HCRTR2 gene is to a deletion mutation, for example, a deletion that corresponds to the deletions found in the hypocretin (orexin) receptor 2 in narcoleptic dogs as described by Lin *et al.*, *supra* (e.g., a deletion of one or more exons, such as a deletion of the fourth exon, that can be caused by  
5 insertion of one or more nucleotides upstream of the splice site of the exon, or a deletion of exon 6, that can be caused by a G to A transition in the splice junction consensus sequence). In another preferred embodiment, the mutation in the HCRTR2 gene is mutation that effects a “knockout” of the entire gene, such as deletion of the first exon as described by Chemelli, R.M. *et al.*, (*Cell* 98:437-451  
10 (1999), the entire teachings of which are incorporated herein). In a third preferred embodiment, the mutation in the HCRTR2 gene is a mutation in an intron, that affects splicing (joining of exons) during translation of the HCRTR2 gene.

In a first method of diagnosing narcolepsy, hybridization methods, such as Southern analysis, are used (see Current Protocols in Molecular Biology, Ausubel,  
15 F. *et al.*, eds., John Wiley & Sons, including all supplements through 1999). For example, a test sample of genomic DNA, RNA, or cDNA, is obtained from an individual suspected of having (or carrying a defect for) narcolepsy (the “test individual”). The individual can be an adult, child, or fetus. The test sample can be from any source which contains genomic DNA, such as a blood sample, sample of  
20 amniotic fluid, sample of cerebrospinal fluid, or tissue sample from skin, muscle, placenta, gastrointestinal tract or other organs. A test sample of DNA from fetal cells or tissue can be obtained by appropriate methods, such as by amniocentesis or chorionic villus sampling. The DNA, RNA, or cDNA sample is then examined to determine whether a mutation in the HCRTR2 gene is present. The presence of the  
25 mutation can be indicated by hybridization of the gene in the test sample to a nucleic acid probe. A “nucleic acid probe”, as used herein, can be a DNA probe or an RNA probe; the nucleic acid probe contains at least one mutation in the HCRTR2 gene. The probe can be one of the nucleic acid molecules described above (e.g., the gene, a vector comprising the gene, etc.)

30 To diagnose narcolepsy by hybridization, a hybridization sample is formed by contacting the test sample containing a HCRTR2 gene, with at least one nucleic

acid probe. The hybridization sample is maintained under conditions which are sufficient to allow specific hybridization of the nucleic acid probe to the HCRTR2 gene. "Specific hybridization", as used herein, indicates exact hybridization (e.g., with no mismatches). Specific hybridization can be performed under high  
5 stringency conditions or moderate stringency conditions, for example, as described above. In a particularly preferred embodiment, the hybridization conditions for specific hybridization are high stringency.

Specific hybridization, if present, is then detected using standard methods. If specific hybridization occurs between the nucleic acid probe and the HCRTR2 gene  
10 in the test sample, then the HCRTR2 gene has the mutation that is present in the nucleic acid probe. More than one nucleic acid probe can also be used concurrently in this method. Specific hybridization of any one of the nucleic acid probes is indicative of a mutation in the HCRTR2 gene, and is therefore diagnostic for narcolepsy.

15 In another hybridization method, Northern analysis (see Current Protocols in Molecular Biology, Ausubel, F. *et al.*, eds., John Wiley & Sons, *supra*) is used to identify the presence of a mutation associated with narcolepsy. For Northern analysis, a test sample of RNA is obtained from the individual by appropriate means. Specific hybridization of a nucleic acid probe, as described above, to RNA from the  
20 individual is indicative of a mutation in the HCRTR2 gene, and is therefore diagnostic for narcolepsy

For representative examples of use of nucleic acid probes, see, for example, U.S. Patents No. 5,288,611 and 4,851,330. Alternatively, a peptide nucleic acid (PNA) probe can be used instead of a nucleic acid probe in the hybridization  
25 methods described above. PNA is a DNA mimic having a peptide-like, inorganic backbone, such as N-(2-aminoethyl)glycine units, with an organic base (A, G, C, T or U) attached to the glycine nitrogen via a methylene carbonyl linker (see, for example, Nielsen, P.E. *et al.*, *Bioconjugate Chemistry*, 1994, 5, American Chemical Society, p. 1 (1994)). The PNA probe can be designed to specifically hybridize to a  
30 gene having a polymorphism associated with autoimmune disease. Hybridization of the PNA probe to the HCRTR2 gene is diagnostic for narcolepsy..

In another method of the invention, mutation analysis by restriction digestion can be used to detect mutant genes, or genes containing polymorphisms, if the mutation or polymorphism in the gene results in the creation or elimination of a restriction site. A test sample containing genomic DNA is obtained from the individual. Polymerase chain reaction (PCR) can be used to amplify the HCRTR2 gene (and, if necessary, the flanking sequences) in the test sample of genomic DNA from the test individual. RFLP analysis is conducted as described (*see* Current Protocols in Molecular Biology, *supra*). The digestion pattern of the relevant DNA fragment indicates the presence or absence of the mutation in the HCRTR2 gene, and therefore indicates the presence or absence of narcolepsy.

Sequence analysis can also be used to detect specific mutations in the HCRTR2 gene. A test sample of DNA is obtained from the test individual. PCR can be used to amplify the gene, and/or its flanking sequences. The sequence of the HCRTR2 gene, or a fragment of the gene is determined, using standard methods. The sequence of the gene (or gene fragment) is compared with the nucleic acid sequence of the gene, as described above. The presence of a mutation in the HCRTR2 gene indicates that the individual has narcolepsy.

Allele-specific oligonucleotides can also be used to detect the presence of a mutation in the HCRTR2 gene, through the use of dot-blot hybridization of amplified proteins with allele-specific oligonucleotide (ASO) probes (see, for example, Saiki, R. *et al.*, (1986), *Nature (London)* 324:163-166). An "allele-specific oligonucleotide" (also referred to herein as an "allele-specific oligonucleotide probe") is an oligonucleotide of approximately 10-50 base pairs, preferably approximately 15-30 base pairs, that specifically hybridizes to the HCRTR2 gene, and that contains a mutation associated with narcolepsy. An allele-specific oligonucleotide probe that is specific for particular mutation in the HCRTR2 gene can be prepared, using standard methods (see Current Protocols in Molecular Biology, *supra*). To identify mutations in the gene that are associated with narcolepsy, a test sample of DNA is obtained from the individual. PCR can be used to amplify all or a fragment of the HCRTR2 gene, and its flanking sequences. The DNA containing the amplified HCRTR2 gene (or fragment of the gene) is dot-

blotted, using standard methods (see Current Protocols in Molecular Biology, supra), and the blot is contacted with the oligonucleotide probe. The presence of specific hybridization of the probe to the amplified HCRT2 gene is then detected. Specific hybridization of an allele-specific oligonucleotide probe to DNA from the individual  
5 is indicative of a mutation in the HCRT2 gene, and is therefore indicative of narcolepsy.

Other methods of nucleic acid analysis can be used to detect mutations in the HCRT2 gene, for the diagnosis of narcolepsy. Representative methods include direct manual sequencing; automated fluorescent sequencing; single-stranded  
10 conformation polymorphism assays (SSCA); clamped denaturing gel electrophoresis (CDGE) heteroduplex analysis; chemical mismatch cleavage (CMC); RNase protection assays; use of proteins which recognize nucleotide mismatches, such as *E. coli* mutS protein; allele-specific PCR, and other methods.

#### PHARMACEUTICAL COMPOSITIONS

15 The present invention also pertains to pharmaceutical compositions comprising nucleic acids described herein, particularly nucleic acids containing the HCRT2 gene described herein. For instance, a nucleotide or nucleic acid construct (vector) comprising a nucleotide of the present invention can be formulated with a physiologically acceptable carrier or excipient to prepare a pharmaceutical  
20 composition. The carrier and composition can be sterile. The formulation should suit the mode of administration.

Suitable pharmaceutically acceptable carriers include but are not limited to water, salt solutions (e.g., NaCl), saline, buffered saline, alcohols, glycerol, ethanol, gum arabic, vegetable oils, benzyl alcohols, polyethylene glycols, gelatin,  
25 carbohydrates such as lactose, amylose or starch, dextrose, magnesium stearate, talc, silicic acid, viscous paraffin, perfume oil, fatty acid esters, hydroxymethylcellulose, polyvinyl pyrrolidone, etc., as well as combinations thereof. The pharmaceutical preparations can, if desired, be mixed with auxiliary agents, e.g., lubricants, preservatives, stabilizers, wetting agents, emulsifiers, salts for influencing osmotic

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pressure, buffers, coloring, flavoring and/or aromatic substances and the like which do not deleteriously react with the active compounds.

The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. The composition can be a liquid  
5 solution, suspension, emulsion, tablet, pill, capsule, sustained release formulation, or powder. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, polyvinyl pyrrolidone, sodium saccharine, cellulose, magnesium carbonate,  
10 etc.

Methods of introduction of these compositions include, but are not limited to, intradermal, intramuscular, intraperitoneal, intraocular, intravenous, subcutaneous, oral and intranasal. Other suitable methods of introduction can also include gene therapy (as described below), rechargeable or biodegradable devices, particle  
15 acceleration devices ("gene guns") and slow release polymeric devices. The pharmaceutical compositions of this invention can also be administered as part of a combinatorial therapy with other agents.

The composition can be formulated in accordance with the routine procedures as a pharmaceutical composition adapted for administration to human  
20 beings. For example, compositions for intravenous administration typically are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free  
25 concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water, saline or dextrose/water. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be  
30 provided so that the ingredients may be mixed prior to administration.

For topical application, nonsprayable forms, viscous to semi-solid or solid forms comprising a carrier compatible with topical application and having a dynamic viscosity preferably greater than water, can be employed. Suitable formulations include but are not limited to solutions, suspensions, emulsions, creams, ointments, 5 powders, enemas, lotions, sols, liniments, salves, aerosols, etc., which are, if desired, sterilized or mixed with auxiliary agents, e.g., preservatives, stabilizers, wetting agents, buffers or salts for influencing osmotic pressure, etc. The agent may be incorporated into a cosmetic formulation. For topical application, also suitable are sprayable aerosol preparations wherein the active ingredient, preferably in 10 combination with a solid or liquid inert carrier material, is packaged in a squeeze bottle or in admixture with a pressurized volatile, normally gaseous propellant, e.g., pressurized air.

Agents described herein can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with free amino groups such 15 as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with free carboxyl groups such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

The agents are administered in a therapeutically effective amount. The 20 amount of agents which will be therapeutically effective in the treatment of narcolepsy can be determined by standard clinical techniques. In addition, *in vitro* or *in vivo* assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided 25 according to the judgment of a practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical 30 compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture,

use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use of sale for human administration. The pack or kit can be labeled with information regarding mode of administration, sequence of drug administration (e.g., separately, sequentially or concurrently), or the like. The pack  
5 or kit may also include means for reminding the patient to take the therapy. The pack or kit can be a single unit dosage of the combination therapy or it can be a plurality of unit dosages. In particular, the agents can be separated, mixed together in any combination, present in a single vial or tablet. Agents assembled in a blister pack or other dispensing means is preferred. For the purpose of this invention, unit  
10 dosage is intended to mean a dosage that is dependent on the individual pharmacodynamics of each agent and administered in FDA approved dosages in standard time courses.

#### METHODS OF THERAPY

The present invention also pertains to methods of therapy for narcolepsy,  
15 utilizing the pharmaceutical compositions comprising nucleic acids, as described herein. The therapy is designed to replace/supplement activity of the hypocretin(orexin) receptor 2 in an individual, such as by administering a nucleic acid comprising the HCRTR2 gene or a derivative or active fragment thereof. In one embodiment of the invention, a nucleic acid of the invention is used in the treatment  
20 of narcolepsy. The term, "treatment" as used herein, refers not only to ameliorating symptoms associated with the disease, but also preventing or delaying the onset of the disease, and also lessening the severity or frequency of symptoms of the disease. In this embodiment, a nucleic acid of the invention (e.g., the HCRTR2 gene (SEQ ID NO:1)) can be used, either alone or in a pharmaceutical composition as described  
25 above. For example, the HCRTR2 gene, either by itself or included within a vector, can be introduced into cells (either *in vitro* or *in vivo*) such that the cells produce native HCRTR2 receptor. If necessary, cells that have been transformed with the gene or can be introduced (or re-introduced) into an individual affected with the disease. Thus, cells which, in nature, lack native HCRTR2 expression and activity,  
30 or have mutant HCRTR2 expression and activity, can be engineered to express

HCRT2 receptors (or, for example, an active fragment of the HCRT2 receptor). In a preferred embodiment, nucleic acid comprising the HCRT2 gene, can be introduced into an expression vector, such as a viral vector, and the vector can be introduced into appropriate cells which lack native HCRT2 expression in an animal. In such methods, a cell population can be engineered to inducibly or constitutively express active HCRT2 receptor. Other gene transfer systems, including viral and nonviral transfer systems, can be used. Alternatively, nonviral gene transfer methods, such as calcium phosphate coprecipitation, mechanical techniques (e.g., microinjection); membrane fusion-mediated transfer via liposomes; or direct DNA uptake, can also be used.

The nucleic acids and/or vectors are administered in a therapeutically effective amount (i.e., an amount that is sufficient to treat the disease, such as by ameliorating symptoms associated with the disease, preventing or delaying the onset of the disease, and/or also lessening the severity or frequency of symptoms of the disease). The amount which will be therapeutically effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, and can be determined by standard clinical techniques. In addition, *in vitro* or *in vivo* assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of a practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

The following Examples are offered for the purpose of illustrating the present invention and are not to be construed to limit the scope of this invention. The teachings of all references cited herein are hereby incorporated herein by reference.



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## EXAMPLES

## EXAMPLE 1 Identification of the Human Narcolepsy Gene

A human BAC library (RPCI11 human male BAC library; see Osoegawa, K. *et al.*, *Genomics* 52:1-8 (1998)) was used. Twenty primers, designed from the  
5 mRNA sequence of the HCRTR2 receptor, were employed to identify clones of interest. They are set forth in Table 1.

TABLE 1 Primers Used for Hybridization

#	Name	Primer Sequence	SEQ ID NO:
1	HCRT2-1-F	TACTACTACTAGGCCACGCG	3
2	HCRT2-1-R	ACACCAGGAGGAGAAAGCTAC	4
3	HCRT2-2-F	ATCGCCTGTAAAGACAGCAAAG	6
4	HCRT2-2-R	AAAGTTACTGAGCCAATGCCTC	6
5	HCRT2-3-F	GAGAGGAGCTTGCAGCATTG	7
6	HCRT2-3-R	AGGAATTCCTCGTCGTCATAGT	8
7	HCRT2-4-F	GAAGAACCACCACATGAGGAC	9
8	HCRT2-4-R	ATCACTTTGCAAAGGGACTGTC	10
9	HCRT2-5-F	GTATGCAATCTGTCACCCTTTG	11
10	HCRT2-5-R	AATGCAGGAGACAATCCAGATG	12
11	HCRT2-6-F	CAGGCTTAGCCAATAAAACCAC	13
12	HCRT2-6-R	GATAAGCCAACACCATGAGACA	14
13	HCRT2-7-F	ACAGATCCCTGGAACATCATCT	15
14	HCRT2-7-R	CTCGGATCTGCTTTATTTTCAGC	16
15	HCRT2-8-F	CCAATTAGCATCCTCAATGTGC	17
16	HCRT2-8-R	GTGTGAAAAGGTAAACCAGGCA	18
17	HCRT2-9-F	CTCAGTGGAAAATTTTCGAGAGG	19
18	HCRT2-9-R	GTTGCTGATTTGAGTGGTCAAG	20
19	HCRT2-10-F	CTTTCTGAGCAAGTTGTGCTCA	21
20	HCRT2-10-R	TACCAGTTTGAAGTGGTCCTG	22

*Initial Study with Large Membranes*

Four out of 5 membranes having the whole BAC library, containing a total of approximately 160,000 BAC clones representing an approximately 10-fold coverage of the human genome, were used in hybridization studies with these primers. Hybridization was performed with a pool of all 20 primers described in Table 1.

*5' End Labeling for Big Membranes*

Oligonucleotides were labeled at the 5' end before hybridization, using fresh (less than one month old) [ $\gamma^{32}\text{P}$ ]ATP (6000 Ci/mmol; 10  $\mu\text{Ci}/\mu\text{l}$ ). The following protocol is adjusted for 4 membranes in 2 bottles, containing 2 membranes/30 ml of rapid hyb. Each. Briefly, a labeling mixture was made of DNA (8 pmol/ $\mu\text{l}$ ) (10.0  $\mu\text{l}$  of the primer pool), 10X buffer (12.0  $\mu\text{l}$ ), T4 PNK (10 u/ $\mu\text{l}$ ) (6.0  $\mu\text{l}$ ), [ $\gamma^{32}\text{P}$ ]ATP (30.0  $\mu\text{l}$ , or 600  $\mu\text{Ci}$ ), and water (62.0  $\mu\text{l}$ ) for a final volume of 120  $\mu\text{l}$ . 20  $\mu\text{l}$  of labeling mixture was used per 10 ml rapid hybridization reaction. Incubation of the labeling mixture was for 2 hours at 37°C, followed by transfer to ice, spinning down, and mixing with the rapid hybridization solution. The membranes were prehybridized at 42°C before the labeling mix was added. Sixty  $\mu\text{l}$  of the labeling mix was added to each of 2 big bottles containing 2 membranes and 30 ml of rapid hybridization solution.

*Hybridization and Washing*

The membranes were hybridized at 42°C overnight. After overnight, membranes were washed with 6x SSC, 0.1% SDS at room temperature; washed with 6x SSC, 0.1% SDS at 55°C in a shaking waterbath, repeated until the radioactivity of membranes was lower than 6k using 1x sensitivity; and washed with 6x SSC to remove the SDS. The washed membranes were put in a cassette for overnight exposure at -80°C with a MR single emulsion film. Positive clones were identified and gridded on small membranes.

*Study of Positive Clones with Small Membranes*

After growing the positively-identified clones on several small membranes (to get several copies of membranes containing the same clones), and washing the membranes, hybridization was performed using pairs of primers, instead of a total pool of primers as before. The total number of hybridizations was ten, using different primers against identical copies of membranes containing all positive clones from the first hybridization. The primer pairs are set forth in Table 2; primer numbers indicate the primers shown in Table 1.

TABLE 2 Primer Pairs Used for Hybridization

Reaction number	Primers Used
1	1 and 2
2	3 and 4
3	5 and 6
3	7 and 8
3	9 and 10
6	11 and 12
7	13 and 14
8	15 and 16
9	17 and 18
10	18 and 19

*5' End Labeling for Small Membranes*

Oligonucleotides were labeled at the 5' end before hybridization, using fresh [γ<sup>32</sup>P]ATP (5000 Ci/mmol; 10 μCi/μl). Briefly, a labeling mixture was made of DNA (8 pmol/μl) (1.5 μl), 10X buffer (2.0 μl), T4 PNK (10 u/μl) (1.0 μl), [γ<sup>32</sup>P]ATP (3.0 μl), and water (12.5 μl) for a final volume of 20 μl. Incubation of the labeling mixture was for 2.5 hours at 37°C, followed by transfer to ice, spinning down, and mixing with the rapid hybridization solution. Membranes were pre-wetted in 6X SSC, rolled in a pipette, and excess liquid drained prior to placing the membrane in the tube. Fifty ml Falcon (polypropylene) tubes were used as container for the hybridization. The membranes were prehybridized at 42°C before 20 μl of labeling mix was added to each tube.

*Hybridization and Washing*

The membranes were hybridized at 42°C overnight. After overnight, membranes were washed as described above. Four clones which were positive for primers designed using the 5' and 3' end of the mRNA were identified. Clone 403B19 was used to characterize the gene.

*Sequencing of Narcolepsy Gene in Clone 403B19*

Shotgun sequencing was used to obtain the gene sequence.

*Preparation of DNA Samples*

5        BAC DNA was isolated using the Plasmix kit from TALENT-VH Bio  
Limited. Thirty  $\mu\text{g}$  of isolated DNA was fragmented by nebulization: a nebulizer  
(IPI Medical Products, Inc., no. 4207) was modified by removing the plastic cylinder  
drip ring, cutting off the outer rim of the cylinder, inverting it and placing it back  
into the nebulizer; the large hole in the top cover (where the mouth piece was  
10 attached) was sealed with a plastic stopper; the small hole was connected to a 1/4  
inch length of Tycon tubing (connected to a compressed air source). A DNA sample  
was prepared containing 30  $\mu\text{g}$  DNA, 10 X TM buffer (200  $\mu\text{l}$ ), sterile glycerol (1  
ml), and sterile dd water (q.s.) for a total volume of 2 ml. The DNA sample was  
nebulized in an ice-water bath for 2 minutes and 40 seconds (pressure bar reading  
15 0.5). The sample was then briefly centrifuged at 2500 rpm to collect the DNA; the  
entire unit was placed in the rotor bucket of a table top centrifuge (Beckman GPR  
tabletop centrifuge) fitted with pieces of Styrofoam to cushion the nebulizer. The  
sample was then distributed into four 1.5 ml microcentrifuge tubes and ethanol  
precipitated. The Dried DNA pellet was resuspended in 35  $\mu\text{l}$  of 1X TM buffer  
20 prior to proceeding with fragment end-repair.

*Fragment End Repair, Size Selection and Phosphorylation*

The DNA was resuspended in 27  $\mu\text{l}$  of 1X TM buffer. The following  
materials were added: 10 X kinase buffer (5  $\mu\text{l}$ ), 10 mM rATP (5  $\mu\text{l}$ ), 0.25 mM  
25 dNTPs (7  $\mu\text{l}$ ), T4 polynucleotide kinase (1  $\mu\text{l}$  (3 U/ $\mu\text{l}$ )), Klenow DNA polymerase  
(2  $\mu\text{l}$  (5 U/ $\mu\text{l}$ )), T4 DNA polymerase (1  $\mu\text{l}$  (3 U/ $\mu\text{l}$ )), for a total volume of 48  $\mu\text{l}$ .  
The mixture was incubated at 37°C for 30 minutes, and then 5  $\mu\text{l}$  of agarose gel  
loading dye was added. The mixture was then applied to separate wells of a 1% low  
melting temperature agarose gel and electrophoresed for 30-60 minutes at 100-120  
30 mA. The DNA was then eluted from each sample lane, extracted from the agarose

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using Ultrafree-DA columns (Millipore) and then cleaned with Microcon-100 columns (Amicon), precipitated in ethanol, and resuspended in 10 µl of 10:0.1 TE buffer.

### *Ligation*

- 5        EcoRV-linearized, CIAP-dephosphorylated Bluescript vector was used as a cloning vector. The following reagents were combined in a microcentrifuge tube, and incubated overnight at 4°C: DNA fragments (100-1000 ng), cloning vector (2 µl (10 ng/µl)), 10X ligation buffer (1 µl), T4 DNA ligase (NEB 202L) (1 µl (400 U/µl)), sterile dd water (q.s.), for a total of 10 µl.

10        *Transformation of Ligated Products*

- The ligation products were diluted 1:5 with dd water and used to transform electrocompetent TOP 10F cells (Invitrogen) using GenePulser II (Biorad; voltage, 2.5 W, resistance 100 ohm). Transformants were plated on LB plates with 50 µl of 4% X-GAL and 50 µl of 4% IPTG, and ampicillin. Transformants were grown  
15    overnight at 37°C, white colonies were picked, grown in a culture of 3 ml LB liquid media plus 200 µg/µl ampicillin for 16-20 hours with shaking. DNA was isolated from the liquid cultures using Autogen 740 Automatic Plasmid Isolation System.

### *Cycle Sequencing of Isolated Plasmid DNA*

- Isolated plasmids were then sequenced using the M13 primers: M13-forward  
20    (SEQ ID NO:23) TGTAACGACGGCCAG; and M13-reverse (SEQ ID NO:24) CAGGAAACAGCTATGAC. For the sequencing reaction, 2.5 µl plasmid template was mixed with 4 µl Big Dye Ready reaction mix (ABI), 1 µl of 8 pM M13 primer, and 2.5 µl dd water. For cycle sequencing, 25 cycles of 96°C for 10 seconds, 50°C for 5 seconds, and 60 °C for 4 minutes were performed, followed by holding at 4°C.  
25    The cycle sequencing reaction products were cleaned by spinning through Sephadex G-50 columns. The eluted cycle sequencing products were then dissolved in 3 µl formamide/dye and 1.5 µl of sample was loaded on ABI 377 automated sequencers. The data was analyzed using Phred and Phrap ( Ewing, B. *et al.*, *Genome Res.* 8:175-

185 (1998); Ewing, B. and Green, P., *Genome Res.* 8:186-194 (1998)), and viewed in Consed viewer (Gordon, D. *et al.*, *Genome Res.* 8(3):195-202 (1998)).

### *Analysis of Gene Structure*

The *hcrtr-2* gene maps to chromosome 6p11-q11. A total of 168,575 base pairs of contiguous sequence was generated for 403B19 which contained all of the *hcrtr-2* gene. Comparison of the cDNA sequence of *hcrtr-2* (Accession number GI:6006037) and the genomic sequences generated allowed deduction of the intron/exon organization of the gene. The gene contains 7 exons which cover 108,439 bp. The first 10 Gs in the mRNA sequence for *hcrtr-2* were not found in the genomic sequence. It is likely that these Gs were an artifact.

The splice junctions of the *hcrtr-2* gene are set forth in Table 3, and the intron sizes are set forth in Table 4. Exon sequences are represented in uppercase and introns in lowercase. All splice sites conform to the consensus GT-AG rule. SEQ ID NOs are given in the column immediately following each site.

Table 3 Splice Junctions of *hcrtr-2*

	Splice Donor Site	SEQ ID	Splice Acceptor Site	SEQ ID
Hcrtr-2 exon1-2	TCCTGGgtgagt	25	aattagTTTGTG	26
Hcrtr-2 exon2-3	CTACAGgtaatt	27	ctctagACCGTG	28
Hcrtr-2 exon3-4	GGGGTGgtaagt	29	tcctagGTGAAA	30
Hcrtr-2 exon4-5	CGACAGgtatat	31	tttcagATCCCT	32
Hcrtr-2 exon5-6	AAAGAGgtaaaa	33	ctgcagAGTATT	34
Hcrtr-2 exon6-7	TCAGTGgtgagt	35	tgccagGAAAAT	36

Table 4 Intron Sizes of *hcrtr-2*

Intron	Nucleotides
Intron 1	73,848
Intron 2	6,322
Intron 3	8,327
Intron 4	13,618
Intron 5	2,730
Intron 6	1,779

The exons do not clearly respect the domain structure of this seven membrane domain G protein linked receptor. Five of the transmembrane regions are by themselves within one exon, two of the transmembrane segments are broken up by introns, and two transmembrane segments fall within the same exon. A survey done one year ago on mammalian G-protein coupled receptors (GPCRs) sequences in GenBank revealed that over 90% of GPCRs genes were intronless in their open reading frame (ORF) (Gentles, A.J. and Karlin, S., *Trends Genet.* 15:47-49 (1999)). Comparison of the intron/exon boundaries of *hcrtr-2* and the genes coding for their most related GPCRs based on sequence similarity showed that the location of the intron/exons boundaries with respect to the transmembrane domains is only partially conserved among the receptors (Sakurai, T. *et al.*, *Cell* 92:573-585 (1998)).

#### Computer analysis of sequence data

Analysis of the genomic sequence of *hcrtr-2* using the program RepeatMasker (<http://ftp.genome.washington.edu/cgi-bin/RepeatMasker>) showed that the sequence containing the *hcrtr-2* genomic sequence is 38.27% repeat sequences and the GC content is 35.3%.

The sequences of the genes were analyzed using the program GeneMiner (Óskarsson and Pálsson, unpublished), which combines the results of 5 exon prediction programs; FGENE (Solovyev, V. and Salamov, A., *Ismb* 5:294-302 (1997)), Genscan (Burge, C. and Karlin, S., *J. Mol. Biol.* 268:78-94 (1997)),



HMMgene (Krogh, A., *Ismb* 5:179-186 (1997)), MZEF (Zhang, M.Q., *Proc. Natl. Acad. Sci. USA* 94:565-8 (1997)) and Xpound (Thomas, A. and Skolnick, M.H., *IMA J. Math Appl. Med. Biol.* 11:149-160 (1994)). For *hcrtr-2*, 3 out of 5 programs predicted the 3' end of exon 1, only one program predicted the 7<sup>th</sup> exon and for the  
5 internal exons, there were at least two programs that predicted each of them exactly or in part.

The promoter sequences of the genes have not yet been characterized. The Promoter Prediction by Neural Network ([http://www.fruitfly.org/seq\\_tools/promoter.html](http://www.fruitfly.org/seq_tools/promoter.html)) predicted promoters that are at least  
10 140 bp upstream of the 5' UTR of *hcrtr-2*, indicating that either a part of the 5' UTR is missing in the published mRNA sequence or the real promoters are not detected by the program.

#### *Analysis of Population for Polymorphisms*

Each exon and its flanking intronic sequences of the *hcrtr-2* gene was analyzed  
15 in nucleic acid samples from 47 patients and 75 control individuals. The patient population consisted of patients of Icelandic and US origin. The control population consisted of Icelandic controls, CEPH (Centre d'Etude du Polymorphisme Humain) individuals from Utah and France, and US samples of various ethnic origins. The African-American/Caucasian ratios were similar between patients and controls. All  
20 narcoleptic subjects complained of excessive daytime sleepiness (EDS). Approximately 66% of the patients had cataplexy, 24% did not and 10% did not have attainable records of cataplexy status. Narcoleptic subjects without cataplexy had Multiple Sleep Latency Tests showing mean sleep latencies of less than 10 minutes and REM sleep in at least 2 naps. Subjects did not take any drugs affecting sleep for  
25 at least 10 days before their sleep studies.

To analyze the nucleic acids, DNA from patient and control blood samples were isolated by the method of Kunkel (Kunkel, L.M. *et al.*, *Proc. Natl. Acad. Sci. USA* 74:1245-9 (1977)). Briefly, white blood cells were lysed in a sucrose lysis buffer, and proteinase K treated; the DNA was then extracted using phenol-  
30 chloroform/isoamylalcohol and then ethanol precipitated. Patient samples that were

- received in the form of nuclei pelleted through sucrose buffer were resuspended in lysis buffer (100 mM NaCl<sub>2</sub>; 10 mM TrisHCl, pH 8; 25 mM EDTA pH 8; 0.5% sodium dodecyl sulfate; 0.1 mg/ml proteinase K) at 55°C for 4-6 hours followed by classical phenol-chloroform extraction and ethanol precipitation (Sambrook, J. *et al.*,  
5 *Molecular Cloning, A Laboratory Manual* (1989)). Samples were incubated at 55°C after isolation for the inactivation of DNase to prevent the degradation of DNA. Concentration of the isolated DNA was determined by spectrophotometric analysis at 260 nm (Sambrook *et al.*, using GeneQuant (PharmaciaBiotech), and samples diluted with sterile distilled water to a 20 ng/μl working solution.
- 10            Primers were designed from intronic sequences flanking the exons of the hypocretin receptor-2 (*hcrtr-2*), using either primer design programs available at primer3 at the Whitehead Institute (<http://www-genome.wi.mit.edu/cgi-bin/primer/primer3.cgi>) or primers for the worldwide web (<http://williamstone.com/primers/javascript/>). The primers are shown in Table 5.

Table 5 Primers Used to Amplify Nucleic Acid Fragments for Analysis of *hcrtr-2* Gene

EX-ON	#	Primer Sequence	Sense/ Antisense	External/ Nested	SEQ ID.
5	1	TTTCTTCAGCTTCAGCTCTCCCTCAGC	S	E	37
	1	TTCAGCTCCGAAGCAGATGACCAGTTG	A	E	38
	1	TTCAGCTTCAGCTCTCCCTCAGCGAGG	S	N	39
	1	CGAAGCAGATGACCAGTTGCGACAAGG	A	N	46
10	1	CTTTCCCACCGCAAATCACCAGTGCTC	S	E	41
	1	ATTTTATTAGAAAACCCCATCCGAGAG	A	E	42
	1	TTCCCACCGCAAATCACCAGTGCTC	S	N	43
	1	TATTAGAAAACCCCATCCGAGAGCAG	A	N	44
15	2	GCATGTACTTAGCATTCACACAGATTG	S	E	45
	2	TCTAATGATGATTTGGCAGTTCATTGC	A	E	46
	2	TAGCATTCACACAGATTGACAGATTCA	S	N	47
	2	CAGTTTGTCAATGCCTTAGGCAAATAT	A	N	48
20	3	TTTGGCAGCTTTGAATTTGCTTATATG	S	E	49
	3	GCTCTTGCAAACTGTATTCACAAATG	A	E	56
	3	CAGCTTTGAATTTGCTTATATGTTGTG	S	N	51
	3	TTGCAAACTGTATTCACAAATGTCAA	A	N	52
25	4	TCCCCTTTGCATACATAATATGACAATG	S	E	53
	1	AAAAAGCACAGACAAAATATTTGGAAGG	A	E	54
	3	ATGCACTTTGAAGAAAAGCATTGACATG	S	N	55
	4	AAGCACAGACAAAATATTTGGAAGGAAT	A	N	56
30	5	CTCAGGCGTCTGGAAGCCTTTCCTTAC	S	E	57
	5	TTAAAGGCTGTTCGCCTTACCTGCTGG	A	E	58
	5	GGCGTCTGGAAGCCTTTCCTTACTGTG	S	N	59
	5	CTGAGTCATCTGGCCTGACAAGGTATC	A	N	60
30	6	GGGTCAGAAACCAATCTGTGGTCAATTC	S	E	61
	6	AGTTGAAGAGTGTTCAATTGATTCTCATCC	A	E	62
	6	AGAAACCAATCTGTGGTCAATTCCTGCAAC	S	N	63

	EX- ON	#	Primer Sequence	Sense/ Antisense	External/ Nested	SEQ ID.
5	6	28	TGAAGAGTGTTTCATTGATTCCCTCATCCTTG	A	N	64
	7	29	GAGTCTACCAAGCTTCCAATAAACTCA	S	E	65
	7	30	GGATAGTTTTACTCAGGTATCCTTGTC	A	E	66
	7	31	CAAATCAGCAACTTTGATAACATAT	S	N	67
	7	32	GTATCCTTGTCATATGAATAAATATTCTAC	A	N	68
	7	33	CACTCAAATCAGCAACTTTGATAAC	S	E	69
	7	34	GTGAGAGATTAAAATAACAAGGGAT	A	E	70
	7	35	CAAATCAGCAACTTTGATAACATAT	S	N	71
	7	36	TGTTTAAACATTTAATTGACACACA	A	N	72
	10	7	37	TTCATATGACAAGGATACCTGAGTAAA	S	E
7		38	GTGAAATAGCCTGAAATAAGCTCAA	A	E	74

PCR reactions were done in 20  $\mu$ l reactions using 40 ng genomic DNA, 0.2 mM solution of the four dNTPs, 0.35  $\mu$ M of each primer (TAGCopenhagen), 2.5 mM MgCl<sub>2</sub> (Perkin Elmer), 1x PCR Buffer (Perkin Elmer) and 0.5 U Amplitaq gold (Perkin Elmer). The primers were used to amplify the fragments by PCR cycling at 95°C for 12 min and subsequently 30 cycles of 95°C for 30 sec, 55-62°C for 30 sec and 72°C for 1 min. The PCR products were prepared for cycle sequencing by incubation with Shrimp alkaline phosphatase (Amersham) and exonuclease I (Amersham) at 37°C for 15 min. After the inactivation of the enzymes the products were subject to cycle sequencing using BigDye Ready Reaction mix (Perkin Elmer) and subsequently run on ABI Prism 377 Automated DNA sequencers. The raw data were basecalled and sequences assembled using the Phred and Phrap software, respectively (Ewing, B. *et al.*, *Genome Res.* 8:175-185 (1998); Ewing, B. and Green, P., *Genome Res.* 8:186-194 (1998)). The Consed viewer was used to analyze the sequences (Gordon, D. *et al.*, *Genome Res.* 8(3):195-202 (1998)). Expansion of a T-stretch in the 3' untranslated region (UTR) of exon 7 of *hcrtr-2* was investigated by amplifying a fragment containing the stretch with a fluorescently labelled primer

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pair using the conditions described above. The PCR product was dissolved in formamide/dye solution and run on ABI Prism 377 Automated DNA sequencers as described above. Allele calling was done using TrueAllele and editing was done using DeCODE-GT (Palsson, B. *et al.*, *Genome Res.* 9:1002-1012 (1999)).

- 5           A total of nine single nucleotide polymorphisms were identified, 7 in exons and 2 in an intronic sequence near an exon. The polymorphisms are shown in Table 6. The base number is according to the mRNA sequence (Accession number GI:6006037). For those polymorphisms marked with an asterisk (\*), the polymorphism is located 5' of the corresponding exons; the numbers indicate the
- 10   distance into the introns.

Table 6           Single Nucleotide Polymorphisms in *hcrtr-2*

	Location	cDNA base #	Nucleic Acid Change
	Exon 1	352	C-T
	Exon 1	355	C-A
15	Intron1	-26*	C-A
	Exon 5	1,170	G-A
	Exon 5	1,177	C-A
	Exon 5	1,201	G-A
	Exon 5	1,246	G-A
20	Exon 5	1,266	G-A
	Intron 6	-87*	G-A

- While this invention has been particularly shown and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without
- 25   departing from the spirit and scope of the invention as defined by the appended claims.

## CLAIMS

What is claimed is:

1. Isolated nucleic acid molecule comprising the nucleic acid having SEQ ID  
5 NO:1.
2. A DNA construct comprising the isolated nucleic acid molecule of Claim 1  
operatively linked to a regulatory sequence.
3. A recombinant host cell comprising the isolated nucleic acid molecule of  
Claim 1 operatively linked to a regulatory sequence.
- 10 4. A pharmaceutical composition comprising a nucleic acid comprising the  
isolated nucleic acid molecule of Claim 1.
5. Isolated nucleic acid molecule comprising the nucleic acid having SEQ ID  
NO:1 with one or more of the nucleic acid changes shown in Table 6.
6. A method of diagnosing narcolepsy in an individual, comprising detecting a  
15 mutation in the gene encoding hypocretin (orexin) receptor 2, wherein the  
presence of the mutation in the gene is indicative of narcolepsy.
7. A method of treating narcolepsy in an individual, comprising administering  
to the individual an isolated nucleic acid of Claim 1 in a therapeutically  
effective amount.

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LOCUS \_\_\_\_\_ 168,575 bp DNA PRI 20-OCT-1999  
 DEFINITION Human hypocretin (orexin) receptor 2 (HCRTR2) gene, complete cds.  
 ACCESSION \_\_\_\_\_  
 NID \_\_\_\_\_  
 VERSION \_\_\_\_\_  
 KEYWORDS .  
 SOURCE human.  
 ORGANISM Homo sapiens  
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Mammalia;  
 Eutheria; Primates; Catarrhini; Hominidae; Homo.  
 REFERENCE 1 (bases 1-168,575)  
 AUTHORS \_\_\_\_\_  
 TITLE Direct Submission  
 JOURNAL Submitted (\_\_\_\_\_) deCode Genetics, Inc., Lyngdals 1,  
 IS-110 Reykjavik, Iceland.  
 FEATURES Location/Qualifiers  
 source 1..168,575  
 /organism="Homo sapiens"  
 /db\_xref="taxon : 9606"  
 /chromosome="6"  
 /map="6p11-q11"  
 /clone="BAC 403B19"  
 gene 1..129,305  
 /partial  
 /gene="HCRTR2"  
 /note="OX2R"  
 /db\_xref="LocusID:3062"  
 /db\_xref="MIM:602393"  
 exon 20,867..21,403  
 /gene="HCRTR2"  
 /number=2  
 CDS join(21,181..21,403, 95,252..95,430, 101,753..101,996, 110,324..110,439,  
 124,058..124,278, 127,009..127,130, 128,910..129,139)  
 /gene="HCRTR2"  
 /note="HCRTR2 exons defined by comparison to mRNA sequence (NM\_001526)"  
 /product="HCRTR2/orexin 2 receptor"  
 /db\_xref="LocusID:3062"  
 /db\_xref="MIM:602393"  
 /protein\_id="NP\_001517.1"  
 /db\_xref="PID:g4557639"  
 /db\_xref="GI:4557639"  
 /translation="MSGTKLEDSPPCRNWSSASELNETQEPFLNPTDYDDEEFLRYLW  
 REYLHPKEYEWVLIAGYIIVFVVALIGNVLVCVAVWKNHHMRTVTNYFIVNLSLADVL  
 VTITCLPATLVVDITETWFFGQSLCKVIPYLQTVSVSVSVLTLSCIALDRWYAICHPL  
 MFKSTAKRARNISIVIIWIVSCIIMIPQAIVMECSTVFPGLANKTTLFTVCDERWGGEI  
 YPKMYHICFFLVTYMAPLCLMVLAYLQIFRKLWCRQIPGTSSVVQRKWKPLQPVSQPR  
 GPGQPTKSRMSAVAAEIKQIRARRKTARMLMVVLLVFAICYLPISILNVLKRVMFGMFA  
 HTEDRETVAWFTFSHWLVYANSAANPIIYNFLSGKFREEFKAAFSCCCLGVVHHRQED  
 RLTRGRTSTESRKSLLTQISNFDNISKLSQVVLTSISTLPAANGAGPLQNW"  
 exon 95,252..95,430  
 /gene="HCRTR2"  
 /number=3  
 exon 101,753..101,996  
 /gene="HCRTR2"  
 /number=4

FIG. 1A

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exon	110,324..110,439 /gene="HCRTR2" /number=5
exon	124,058..124,278 /gene="HCRTR2" /number=6
exon	127,009..127,130 /gene="HCRTR2" /number=7
exon	128,910..129,305 /gene="HCRTR2" /number=8

BASE COUNT 55,308 a 29,672 c 29,838 g 53,757 t

CGACTTGATTTTATTTTTTGCATATGGATATCCAGTTTTTCACAGCACTGCTTGTTACCTT  
CAGCAAAGAACAGTTGTCTGTAAATTCATGGGTTTATGTCTAGGCTCTCTGTTCTGTTCT  
ATTGGTCAACATATGGTCATATATCACTTAACTGCAGGGAAGGGATACATTCTGAGAAAT  
GCATTATTACATGATTTTCATCATTGTGCAAAACACTATAGAGTGTAGTTACAGAAACCTAG  
TATCTCTAGCTGTGTTCTTATGATTCAAATTTGCTTTGGTCATTTGAGATCCATACTGGT  
GGAGTCTAATTATTCAAACCTAGGGAAAACAGACAAACAGAAAAAACTAAGACCAAGTTA  
GCAGAAGAAAGACAATAACAAAGGTTAGATCAAAAATAAATAATATAGAGAATGAAAAAA  
TTAGAAAAAGTGGACAAAACCTACAATGTACTTTTTTGAAAAGACAAAACAAAATTAACAAA  
CCCTTACCTTGACTAAAAAAGAGACTCAAATAAATAAAATTTGGAATGAGACAGGAGAC  
ATTACAATTGATGTTAACAAAAAGATCATAAGGTACTATTATGAACAACTATACACCAAT  
AAATTGGACAACCTAGAAAAAAATGGATAAATTCCTAGAAATACACAGTCTATCAAACCT  
GAAACAAGAAGAAATAGAAAGCCTGAACATACCAGTAACAACCAAGGAGACTGAGTAAAT  
AATCAAAAACCTCCCAAGAAGAAGAGTCTAGGACCAGAAAGTCTTCACAAATGAATTCTAC  
CAAACATTTAAAGTATTAATGCCAATCATTCTTATACTCTTCCAAAAAGAAAGAGG  
GAATATTTTCAAACCTATTTTATGAGGCCAGCATTATTCTGATACCAAACTACGCAAAA  
ATACTACAAGAACATAAAAACTACAAATGTGGGAATTATCATGTATACATATGCAAAAAAT  
CCTCAGTAAATCCTAGCAAACTAAATTCACAGTACATTAAAAAGATCATATAGCATGA  
CCAGTGAAATTTCTCCTTAGGACGCAAGGATAAGTCAACATATAAAATTTGAATGTGATAT  
ACCACTTTAACAAAATGAAGGATAAAAATCATATGATCATCTGAATAGATGCAGAAAAAG  
CATATAACAACTTTGACGTTGTTGAGAAATTGAAAGCTTTTCTCTAAGATCAAGAACAA  
AGCAAGGATGCCCATTTCTGCTTCTATTAGCATAGTGCTTGAAGTCCTAGTCTGGACAA  
TTGGGCAAAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAA  
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TCTCATGTGTAGACAACCTTAAAGATTCCACAAAAACAAACAAACACACAAACAAACAAA  
ATAGCTAGAGCAAAGAAATGAATTCAGTACAGTTGCAGAATGCAAAATCAGTATACAAAA  
AGTACTTGTAATTTCTATATAATAGCAACAACTATTTTATAAGGAAATTAAGGAAACAAT  
CCCCATTACAATAGCATCATAAATAAATAAATCTTAAGAACAATTTAACCAAGGAGGTGA  
AAGACTTGTGTACTGAAAACCTATAAATGCTGATAAAAAAATTAAGAAGATACAATAAA  
TGGAAGATATTCATGCCATGGTTTGGGAAGAATTAATATTGCTAAATGTACATACTACCC  
AAAACAACCTGTAGAGTCAATGCAATCCCTATCAAAATACCAATATTTTTTTTTTTTACAG  
AAATGAAAACACAATCTTAACACTATTTAAACCAATTAACAAACCTATGATTTCAATTT  
GGTCAAAATGTGTTAGAATGGATTTCTTTTATTGTTTTGAACTTGTCTCTTCCAAATTTCT  
AAAGCCTGGTTCCTAATTTTTTACTTGAAATACCAAATAACAAACCCACTTAATGAGCTCT  
GAGCCAGTTTTAGTAGCCAACTTGTATTTAAATAGTGTGTTACATATTTGCACAAAAAG  
CCAACGGAGTCTAAATCAACACTAATTCACATCATTACTAGCAATCTAAAACATCAGATG  
ATAATTTTGCTGTTGTCTTTTCAGGCAAGATATTCAACCATTGGTATTAAATGTTTTATAT  
GAATGTGCGGTGTTTTATTTTCAGAAACACTTCTCTGAATTTCCCAAGGCCTAAGAGCTATT  
CATCATAGAGGTTTGTGGAGGCGGTAGTTAGACATTTTCTACATGCATAATGTTAATTCA  
TTCAAACATTATAGAAAAAAAGTTTGTAAAGAAGTTAATTTTCAAGGTGACAAAAAAATC  
AGATTGAATCATGTTTATTTTATTTCAATTTAAACTCGTTGGCTATCTTAGGAAATTCAC  
ATTGTTTTTGAAGAATATATGAACAAAGTTTGATTTCATCTTATCTATATAAGCATGAGAG

FIG.1B



FIG. 1C

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ACAAAAACAAAAACAGCACATCCGCACAAAAACCCCATCTGAAGGTCACCAACACCAAAT  
ACCAAAGGTAGATAAATCCACAAAGATGGGGAAAAACAGCACAAAAAGCTGAAAATTC  
CAAAAAACAGAATACCTCTTCTCCTCCAAAGGATCACAATTCCTCACCAGCAAGGGGACA  
AAACTGGACAGAGAATGAGTTTGATGAATTGACAGAAGTAGGCTTGAAAAGGTGGGTAAT  
AAACTCCTCTGAGCTAAAGGAGCATGTTCTAACCCTAATGCAAGGAAGCTAAGAACCTTGA  
AAAATGGTTAGAGTAATTGCTAACTAGAAATAACCAGTTTAGAGAAGAGCATAAATGACCT  
GATGGAGCTGAAAACATAGCACAAAGAACCTTCGTGCAGCATACACAGGTATCAATATCCA  
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GGAATATGTGAAAAGACTAAACCTACATTTGATTAGTGTACCTGAAAGTGACGGGGAGAA  
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AAAAACAACCCCAAGACACATAATTGTGATGCACCAAGGTTGAAATACAGGAAAAAAG  
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CTATAGAGACTTAGACTCCCACGTAATAATAGTGGGAGACTTTAACACCCCACTGTCAAT  
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GAATACTATAGACACCTCTATGCAATAAACTAGAAAACCTAGAAGAAATGGATAAATTC  
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CCCTTTAAAAAAGTGGCACAAGACAAGGATGCCCTCTCTCACCCTCTATTCAACATAGT  
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CATTGTCTCAGCCCAAAATCTCCTTAAGCTGATAAGCAACTTCAGCAAAGTCTCAGGATA  
CAAAATCAATGTGCAAAAATCACAAGCATTTCTATACACTAATAATAGACAAACAGAGAG

FIG. 1D

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CCAAATCATGAGTGAACCTCCATTCAAATACCTAGGAATACAACCTTACAAGGGATGTGA  
AGGACCTCTTCAAGGAGAACTACAAACCACTGCTAAGGAAATAAAAGAGGATACAAACAA  
ATGCAAAAACATTCCATCCTCATGGATAGGAAGAATCAATATCATGACAATGGCCATACT  
GCCCCAAAATAATTTATAGACTCAATGCTATGTTTCATCAAGCTACCACCGAATTTCTTCAC  
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AGGCCAAGGCAGGAGGATCAAGAGGTCAGGAGATTGAGACCATGGTGAAACCCCGTCTCT  
ACTAAAAATACAAAAAATTAGCCGGGCGTGGTGGCAGGCGCTGTAGTCCCAGCTACTTG  
GAGAGGCTGAGGCAGGAGAATGGCGTGAACCCAGGAGACGGAGCTTGCAATGAGCCAAGA  
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AGCAGAATTGATCCTGCAGAAGAAAGAAATAGTAAATTTGAAAACACTCTATTTGAAAAT  
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AGAAAATAGCCTCAAAAGCATAAATCTAAGAGTTACTGGCCTTAAAAAGGAAGGAGAG  
AGAGAGAGAGTGGGATAGGGGTAGAAAGTTTATTCAAAGGGATAACAATAGAGTATCAGT  
ATTCAAATACAAGGTTATGGAACACCATTCAAGATTTAACCCAAAGAAGACTACCTCAAGA  
CATTTAATAACTGAACCTCTCATTCAATGGGAAAAGTAAAGTCCTTTCAATAAAGGTGTTG  
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CCCAAAATAGATTAAAGACCTAAGTATAAGAGCTAAAACCTATGAAACTCTTAGAAAGAAA  
CACAGTAAATTTTTGTGACCTTTGATTAGGCAATGATTTCTTAAATATGATAAAATATGG  
TAAAAGCAACAAAAGAAACATGAATAAATGGATCTTATCAAAATTTAAAACCTTTTTTG  
CATCGTAGAATACCTATCAAGAGTATGAAAAGAAAACCTACAAAATAGGAGAACATGTTTG  
GAAATCATGTATTTGTTAAGGGATTAGTATACAGAATATATATATATATATATATATA  
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CTAAAAAATAGGCAATAAATAGCTATTAGTTCTCCAAAGTACATACACAAATGACCAAC  
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ATGATATTAGACATGGATTTGTCATATACAGACTTTATTAAGTTAGATTCCCTCTATGCC  
TAATTTGTTGAGAGTTTTTATCATGAAGAGATGTTGCATTTTGTCAAATGCCTTTTCTGT  
GTCTTTTGAGATGATCATATGGTTTTCTGCTCTTATTTTGTCTGATATGATGTACCACATT

FIG. 1E

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TATTGATTTGCATTTATTGAATCATCTTCCACCCCTGGGATAAATCCCACCTTGATCATG  
GTGTATTATCTTTTTGATGTTTTTGGATTCACTTTGCTGATATTTTGTGAGGATTTCT  
GCATCTATAATCATTAAAGGATATTGGCCTGTAGTTTTCTGTTTTTATGTTGTATTCTAGT  
CTGATTTTGGTATCAGGGTAATGCTGTTCTTGTGAGCGTGTGAGGAAGTCCAAAAGACT  
TCTTCTTTAGTGTTTTTGGAAATAGTTTGAGAATTGTTAGTTTTTTTTTTTATAAGTTTGG  
TAGAATTCAGCAGTAAAGCCATCCAGTTCTGGGCTTTTCTTTGTTAAGAGACTTAAAACA  
CACACAACGCACACACAAAATGAAATATCACTTTCCACCCATTATAATTTACAAAGTGGA  
AAATAACTCGTGTTGATAAGAATGTGGAAACCTTGAAACCTTCATGCATTGCCAGTGGTA  
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ATTAATACTATTTCAGCCACAAAAATAATAAAGTACGGATAGACACTAAAACATGGAAGA  
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CTTTCACCATAACTATATGGAGTTCATTGTATGTATATTTATTAATAATGGAATTAAGATG  
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CCCCTGGGACTGATGTTTGAAAATACACATATTTTGCTCCTACTCTTTCCTTCCCCAGAT  
CCCACCCCTCAGAGCACCCGACGATAATGGATAGTTTCTAGCAGGGTGTCTGGAATGGGC  
AAGTACCCCAAGTTATAGTTTGTACTGCAAGACTTGAACCCACTCTTTTCTGCCCTC  
TATTATTATTTTTGCATTTTAACCATTTATTATTTTGAAGAAAAGAGAATTTTAGAA  
TATGGAAAGAGGAAGTGAATTAATAAAATAGCACACCCTACATAGAGACTGCTAATCCAT  
CTCCAGTCTAAAGATTTAGTAATAGGCAAGAATATACATATCCAGGAATTTCTTGGTGT  
TACATAAACAAAGGCGGCACATATGTATATTTTTTCAAAAATATTCAGTGTGGAAGAAG  
GAATTACTCCCTTCAATTGAGTTCAGGCCTGATCAACAAGTAGTGATTGGCCAACAGCTA  
AATGCAAAAGTGCATAGCTAAGTCTGGGGATACAAAGATGAATGAGAAAACATTTATGCCCT  
TAGGAGAAAAACAAATATCTTTATCTCAGAGAATAGAGAAGGAGATTGATTCTCTTTGGG  
GGAGATGTCATCCTGAAGAGTATAACAAGTTCCCCTATAATTCTACTTTTCAGTACTGTT  
TAAATACAACTGGATTTTTTTTAAATATGTAAATTTATATAATTTTACAAATGTCTTTG  
TTAAGAATTAAACTATCATTAGTAAAGGACACAGCTGGAAAATTGAAAACATTTTGGTT  
CTCTACTGTGGAACAGAATAGAGTAACAGCAAAAAGCGTATTTCTGGAATTGGACCCTG  
ACAACCTGCTTAAACACTCCACCCTTTCTAGCTATATGACCTTGGGTAAGTTACTTAA  
CTTCTTTGTGTGTCAGTTTCTTCATTTGTAAATTTGGAATAATAGATGCTTTTTTTTGAGA  
CAGTGTCTCATTCTGTTGCCCAGGCTGGAGTGCAGTGGCGTGACCACAGCTCACTGCAGC  
CTCAACCTCCTGAGTTCAAGTGATTCTCCAACCTTGAGCCTCCAGATAGCTAGGACCACA  
GACACATGCCACCATGCCTGGGTAATTTTTTTTTTAAAGTTTTTCATAGAAATAGTGTCTC  
ACTAAGTTGCCAACCTGGAAAATTGGAATAATAATTCATAAAATCTTCTCCTAGATTT  
GTGAAGATCAATTGAGTTAATGTATGTAAAGTACTTGGCACAGAGCTTGGCCCATGTAAT  
CTCTCAATGAGTGCTAACATTACTTGTCTCACAAAAAGTTACTTACTTCCGTCTGGCACC  
AACTCCCTCTCTCACTTCCCACAATCTGGTTACCATTCACTTCTCAGTTCTCAGCTTAAA  
CAATGTCTTTTCCATATGGTTTCATTGACGCCACTTTGGGAAAATAGATGTCTCTTCTGC  
TTGCATTTTCAGACCTTTTATGGTGTATACCTTAGGGCATTTGCTTTACTGACCAAAAT  
ATTTGCCGGCTACTCTGTGCTTTTCATGACACACTGAATAAGACAGGAAGAGTGTATATC  
TATGCTCAACATAAGATAGGCATATAATGGAAGCTTCGTATATATTTGTTGAATAAAAA  
CATAAGGGGAAAAATATCAGATCTAATAATGCAGGACAGGAGGCAAGATGGAACGGAGAGA  
ACCTTGTCTGAGAAGAGACATAATTAACAGGGCATGGGAGGTAATAGAAAGATTGGAG  
GAAAAAGAGACAGAGAGACAGAAATGTTTGTGTAATTTGTGACAAGTAGCTTTGATTGT  
TCATGGCCTAATCTTTTAGGGCATGAGGTTATTTCACTCTGTAGCCCACCGAGAGTGC  
GTACAGTGACACATGTTATGTAAGTCCCTTTTCCCTTTTATAAATGTCTAGACCCCT

FIG. 1F

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GTGATTTGAGACTTTTCTAGAAGAATTTAGCTGAAGACCATATTGTTTTTTAAATGTAGT  
ATTTGGAGCCTAGAGGTGCCAGATAACTTCCTGCAAAGCTAATGCATTTATTTTGGGAAT  
ATATAAGCTCAGTATCATCATTACCAACAGTGCTCAGACTTGATTTTATTTTCATTCCAA  
CAGCAAAGGAAAGAAAGCAACTTCTTTCATGCTTCCATGCCACTCTGCATCTCTCTACCT  
TCACAGAGTTTCTCAATAATGGCAACATTTCCAGTTCACCAATGGACTGAGAGATCATTG  
AGGCTAGACTAGTCTTATTAATCCTTATACCCAGCTCCTAGCCGAACCTCTGGACACAC  
AATAGATACTCAGATACATTTACTGAAATGCATATAGAAAAGTTACACCTGCAAAAAGAT  
GATCTCTCACCAGGAATAAGAAAAATATAATCTGGGACAGCCCATATATGAGATCTCTAAA  
CAACCTACCTATAACCACCAAGAAAAAAAATACCTGAGTTTGAGATTTATTTTCCGTC  
TCATTTTTAATATATTCCAGTTAGTGAAAGAGCTAAAATAAATGACAAGAAAAATTTAAT  
CTAGGTATTTAAACAGAATTATTCTGAATGTTGTGAGCTACATTTCTTTTTTACCTTTTA  
TTTATACATAGTATTTGTATATACTTATACAATATATTTATTTTGTATATATAAATATAT  
TGTATTTATTTATACATGTAAATGTATAATATATTTATTTATACATAGTATTTATATATA  
CATAGTATTTGTATATATTTATAGGGTACATGTAATATTTTGTACACGCATAGAATGTG  
TAATGGTCAAGCCAGAATATTTAGAGTATCCATTACCTTAAGTATTTATTATTTCTCTGT  
GCTAGGAGCATGTTAAGTCTCTCTTTTAGCTATTTTGAAATGTACATTGATGTTAACTA  
TCATTAACACAGAGTAATTGATATGTATAGCAAATAATATTTGCAGTAGGATATCACATG  
TTACTTATTTATTTATTTATTTATTTTATTATACTTTAAGTTCTAGGGTACATGTGCA  
CAACGTGCAGGTTTGTACATATGTATGCATGCGCCATGTTGGTGTGCTGCACCCATAA  
CTCCTCATTTACATTAGGTATATCTCCTAATGCTATCCCTCCCCCTCCCCACCCACAG  
ACAGGTTCCAGTGTGTGATGTTCCCTTCTGTGTCCAGGTGTTCTCATTGTTTAATTCC  
CACCTATGAGTGAGAACATACGGTGTGTTGGTTTTTGTCTTGCGATAGTTTGCTGAGAA  
TCATGGTTTTCCAGCTTCATCCATGTCTCTGCAAAGGACATGAACTCATCCTTTTTTGGC  
TGCATAGTATTCATGGTGTATATGTGCCATATTTCTTAATCCAGTCTATCATTGTTGG  
ACATTTGGGTTGGTTCCAAGTCTTTGCTATTGTGAATAGTGCCGCAATAAACATATGTGT  
GCATGTGTCTTTATAGCAGCATGATTTATAATCCTTTGTGTATATACCCAGTAATGGGAT  
GGCTGGGTCAAATGGTATTTCTAGTCTAGATCCTTGAGGAATTGCCACACTCTCTTCCA  
CAATGATTGAACTAGTTTACACTCCCACCAACAGTGCAAAGTGTTCCTATTTCTCCACA  
TCCTCTCCAGCACCTGTTGTTTCTGACTTTTTAATGATCGCCATTCTAACTGGAGTGAG  
GCACTGGTCTGAAAATATCAATTCATTTAATTCTTTTAAACACCTTAAGGGGATATCATG  
GTACAATTTAGAGCTTTCTTTTGTGTTTGTAAAATGGATTGATTCCTTTTCCCTACATC  
CAGCAGAAATATTTGAATTGAAGAGAAGAGTAATACCTAAGAAGTAGAAATTCCTTTCTT  
ATGTTTTCAAAGATATCAAAGATCTAAGGAAGATATTCACATCAAAAATGAGTATTATA  
ATATTTATTATCTATGGTGCATTTGCAAAAAAGAAAACAAGTAATAATCTGAAGATTTAA  
GTGAATATTTTATGACATTGGAGTACCACATATTTAGAAGAAAGCACCAGAGAAATCATA  
GATAGAAGGAAATGGAATATTTGTAGGATCAAGATAAATACAGCTTGTCAAAAATAAAG  
CAGGTATCAGGATAAAATCTTGAAAATATTTTTCATTTCTCGTTATTTATAACTTCAATTT  
ACTGTGATGATTAATTGTAGGTGGAAGATTTACGAAGAGAAGACTGAAGTATAGACAAGT  
TGAAGTGCCACAAAATGAAAGCTAATGACACTGACTACTTAGGAAATAGCAGACTGGGTC  
CATATTTATAGATTGTCAATGACAAGGAATTTGCAGATGTTAATGAATATAGATCCGAAC  
TTAAGTTGCAACAACCTTTCCCACTTTGAGATGAATAGTGCATGGAAGAGTAAAATGCAG  
ATGTTAATAAATCAGAGGAAGACATCGTGCCAGAGTATAAAGTTGACAGATTTATGCCGA  
TGAACCTGAAACAAAGCCACAGAAGGCCTACTTGTCAAATTTACTGGTGACAACAGGTCTG  
GAGAAATGGCTAATGTTTTGGATAATAGCATTAGAATTTAAGGTCTGTTTAACTTCAAA  
TTAACAGAAATGAAATTAATATATGCACATATCAATTGGGTCTTTTGCTTATATATCATCT  
CTTAATAGAGCCTTTTTGAACAATCATTTCTAATGTGACCTTTGGGATTTTCTACTCATC  
ATCACCTCATCCTGTTTGGTTTGCATTATAGCATCTATCCCTTCCTAACGTTTTCCCTAT  
GTATTTGTTAGTTTGTGTTTTTTTTTAACTTAACTTACTAGAAAGTAAAATGCATGGAAAC  
AGCAACCTGTTTAACTTTGTATCACTAAGAGTGGAATAAATACCCCTCAGGAAATATTTGG  
TAAAATAATAAATGCCATTGATGCCCTTCTCTTAAAAAGAAATTTAATTAGTGCAGAT  
TGGGGAAATACAACAATATTTCTCATAAAATGTGATATCTATACAATAACAGAAGTACTA  
TGTCCCAAAAAGTATTCTATAAATAGAAGAAAGAACAGATGGTTTTGCTGCTGATTAATC  
CATTTATCTTTTCGTAAATCATCTAATTTCCCCAGGAACAGCTTCCTCATCTATTAAAGGG  
GGTTAGTAATAGCTAAGCCCTCAGGGGTTTAAAAATGCATATGAAATAATTTTATAAAC  
ATAAAGCACAAAATATGAAAAATGATGATTGGAGGAGGGGGTGGGGTAGTTAACTA  
AATCTCAGTGTAACCACCAATGTCTGTGTGTGTGAAAAAATAATTACATATAAAAAAC  
TGTTGTCATCCAAAGAATAATGTACTTTTTGCACTGGCAAGACTCAAACCATATTATTGT

FIG. 1G

TACTTCCTCCCAGTTACATATTTTGCAAGATATTGACAATTGTCTAAAGGAAGACCAAAC  
AGATGTAGGTGGGAGCTACTGTCATTTGAACAACATTGAAAAGAAAAATACTAAAAAGA  
AACATGAGGGCATATAAAGGAGCGCTGGGGCTGTGATGTTTATTTTGAATCTGTGAAGCA  
TTGTTCATGTGGAAGATTTATTCTGTGTAGCACCAAGATGCAAACTAGGAATTAGAGGTAA  
AAGTCTCAAAAAGACAAATCGTGGCTTGAGACCTTGGTTTAAATGTAAGAAACAGTTTTCT  
CACCCCTTAGAGCACTCCCATAGGATGGAAGTAGTGAATTGTGGTGGTCACATTCAGCT  
AGATGGGGACATGTCAGCAATGTTATCAGGAGGCTTCTACTCTGAAGCTGAAGTTCAGAC  
AAGATTTCCAGGCTCTTCCCAAGTGCAAGATTGTAATTACTTAAATGCAATATTTTTACC  
ATGTTTATTAAGAATAAAGGATCATGAATTCACATTCTGACAAATGCTAGAACTACTTAT  
TATTAGAGACAAAACAGTGCATGAGAGAATGGCAGGTGACATCAGCCCTGAATCAATGG  
GAAGAAAGACCCAATGGGATGTGGTATTTACCAGAGAGAGCACTTCTGCTTAGATTGCTA  
CATCCTACAGTGAATGTTTAAATATCATTGAGTATATTGGTGGTCTGTGATGCTTGACAAC  
ATTAACATATGATCATATTTATGACACTTGGCGTCTTCAAGAATTTGTAGCTCTATTTCA  
CATGACACTTAACATATCGCAAATACAAATTCAGCTAAATAGACCCTTCAGTTTAAAAAC  
AGTCTCATTTCTCAAATTTTAAAGGAGAAAGTGAAGACGGAGATGTCTTAAAGACTCGGCAA  
GTACTAAGTTGGCAAATGTCAAATGTTAAATAAGTTTATATTAATGTTAAAGTGTGTTG  
CCTGGAATGACTTTTCCATTGTCTGCTTGAGAAACACAGAGGCACCTCCTTATGCTTT  
TATATTTGCTTTTACAAAGACAAATGTATCAACATGCTCTGTATTAATTGTATGTTGACAT  
TTTTGTTCATATCCACAGACTGATGCATGTCTGTGCATGGTTTATAATAAGTGCACGTAAA  
AATAGAGAAAATAAGTAGAAAAGAGAGAGATTTAACTCTCACCCCCCACCCTTATGCTTT  
AACAGATTAAATTAGTTTTCTACTTTTTTTTTTTTTCTTCAGCTTCAGCTCTCCCTCAG  
CGAGGGAGGAGGCTGTGGGCTGCGGACTGAGTGCTGGAATGAGGAGTAATTGAGCTTCAG  
CTGAGCCCGACGTAGCTTTCTCCTCCTGGTGTCTGCTGTCAGCCTCCAGTGCCGGGTCC  
CTAGTTCTCAGCTGCCTATCTTCCCGGTGCAACATCGCCTGTAAAGACAGCAAAGCCAC  
CGCAGAAGTTGCCCGGCAGAAGACTCCGGAGGCATTGGCTCAGTAACTTTTCACGTCATT  
TTCTGCTCGGGAGCCCCCTTCTAGCCTCTCCGCGCAGCCTTCCCACCGCAAATCACCAGT  
GCTCATGGGGCAGGCGGAGAGGAGCTTGCAAGATTGAGCGGAACCGGACTTGAGCCCGTG  
ATGTCCGGCACCAAATTGGAGGACTCCCCCTTGTGCAACTGGTCATCTGCTTCCGGAG  
CTGAATGAAACTCAAGAGCCCTTTTAAACCCACCGACTATGACGACGAGGAATCTCTG  
CGGTACCTGTGGAGGGAATACCTGCACCCGAAAGAATATGAGTGGGTCTGATCGCCGGG  
TACATCATCGTGTTCGTGCTGGCTCTCATTGGGAACGTCTGGGTGAGTCTCTCCCGGG  
CAGCCCTCCTAGGGGCTATCACCCCTCTCCGCCCGGGCTGAGAAGGCTCTAAAGAGAC  
CCCTCCCTCCCCCGGAAGCAAACAAAGAGGTGCTGCTCTCGGATGGGGTTTTCTAATA  
AAATAAATAATAATAGAAAGTTTTCTGATTTTCCGAACCGGGACCGAGCCCTGGAAAG  
GTTATTCCCTGTTTTGTCAGGAATAACGGGGAAACCGGTTTTCTTTTTTCGAGCACCTAGAT  
TACAAGCGCAGGGAGAGGGGCGCGGCAGGGATCTCCAGGTGGATTTTGTGAGTGTGTG  
TGTGTGTGGGTGGGTAGGTGGGGGAGTCACTCATCCCTTTGTGTAACGTGGCTGGGTGTT  
TCAGGGGGGTTGGGACGAGACAGAGCTTGCAAGATACAAAGCTACATCCCTAAGGAGCAA  
GCTCTCTGTGGCTGTGGAAGTCACAAAGCATTTGTGAGCTAGGTGGCATTGCCCTTTGGC  
GAGGAGGTTTAGTCTCCAGTCAAGAGGTGGTAATGAACCAGCAGGGAGTGGAGACGGAGG  
CAAAGCAGGGAAGTGCACCTCACTCATAGAAGCTGAATTAACAGGATCCATGCCTGGAGC  
AAGAAGGAGGGGCATCGGAGAAAAGTACCACAGAGATCTCAATCATCCATCCATCCATT  
ATTCTTACATCCATTACGCCAATATTTTTTTTTTTTTCAGTCTGCTTGTGCGAGGCTCAG  
GAATTATTTCATGTCAACTGTTTGTGTTGTTTGTGTTTGTGTTTGTGTTTCTCCAAAGATGA  
GACTAAGCTTAATGCTAGGCTATTTGTCCCGGTCTAGGTCTGTATGCAACACGGGTTTT  
CTCGACCCCTCATCCCCCTCCCCCTAAACAATTTCTGAGGGTTGGGGAGGGGGTGAGATG  
GCAACATGGTGAGTGCGATGATGGAATGTATTAGGGCAGTTGGGGAATATACCTCCAGAA  
AAGGGGCTTTGGAAGGGAGGGATAACTTGAAATAAATTTGTGAATGGAAGGAGAGTGTACC  
TTGATGAATGAAGAGTAGAAGGCTGGGAGACTTTTACATGCAGAGGGCAGTGTGGAGGA  
AGTCTCTGCTGAAAATGACAGGAGATGGAGGAGGCTAGGAGTTGCTCTTGATTTTCAATTT  
ATAAAAGAAGAAGGTGAGTGAGGTGAGATAGGCTGGGAGGCTTTGCAGTCAAAAGCA  
AAGAACTTGTAGCTGCAATGGGACTGACAAGGAAATTTATCAGGCTTTTCACTAACCTG  
ATTTTTGCCTTCTCTCCCAAGTGTGTTGGTCTGGGTAGAAATCATCCCGAGTAGTCTCTC  
ACCAACTCAGCAGGCAGAATAGATGATAGTATGTGAATGACAGGAGTTCTCCAGAGTGT  
GGTAGAATGTTATTTGAGGAGACAAGAAACCTCTGAGAACTTTAGTACATTTTTAAATAT  
TATTTTTAGACTGTTTTCTTTGGTTGATTTAAAGTAAAAATAAAGGAAATCTTTTTGG  
GATACTAACAAAATGAAACAAAAGTGGAAATACACAAGATTAGGATTCTTGTATTAAGCA

FIG. 1H

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TAATTCTGTTGATAATAATCCTAATCTTGCTTTCTTCTTCTTGTACCCATCCTTAGGA  
TTACATCTCTTAAGACACATGGCTACCAGCATAGCAACATTTTACTGCATTATGCCAACA  
CTTATTGATAAGTGAATAATCAAAATTGAACATATATTGAGTACCTACTGTGTGCCAGAG  
CCCTTCATGTACATTCTCTCCCTTAAATATCAAAATAACCCACATTAGCCAGAAGAAGAA  
ACAAGACTTAGAGAAATAAAATGACGTATTAAGGGACATAATTTAAATTCAGTTCCATTT  
TTTCTGACCTCAGATCCAGAATTCTCCATTGTTATTCCACTCTAGAGCTAAAAAGCATAT  
AGAGAATAGATTCTCTGCTCCTGATTGTCTGCAAGTTTATTAGATGTGTTCTGTTCTCC  
TCTGCATCAACGCCCACTGCCAATAAAGTACAATGAGGGATTAATGGCACTGTCAATTCTC  
TTCACCAAAAACCTTTCCAGAGAAGCAGTAATTTTTTTATGAATAGCTATCAATAGTAAC  
TATTTGCCTTCCTTATTTTAATTTTCGGCTGAATCTTTGTGGTAAAATGTGCTCTTCTTT  
GTTGTTATTGCAATTTTACCTTGCATAGACCTTGTAAGTGAATAGTCTCCATATCCTAATT  
GCATAGTTTAGGGATACATGTTTGTAGCCTGGGGAGTTTATGTTTCAAGAAGGAAACAC  
CTCTACAGTAAGGCTACTTGTTCATAATGTCAAGGAAGATAGCACTGTCCACAGCCCCA  
AGTGCTGAAATGGCCAATTCCATTACGCCTAAAAAGAAAGATTTACTCAAAGCACTCTGC  
CTTAAGAAGAACTGACAGCTATTTTCTCAGGACTGAATAACACTGAAATCCTCTCTGGTT  
GAACTGAAATGCATTCTTTTCTGACATACTGCCTGAAAGTTGATGAGGTTTAGGTTTGAC  
ATTTAAACAAACGAGTAGTGTCTGTTACTCACAGACAACCTCCTGCTCTTTGATGTCACTG  
TCAAATTTGCAAAATGAATTAGATTGAGAATTGCTTCTTTGCCCCCTGGGTATAAGTAAT  
TTTGCACATAGAGTGGTAGGACAGGATGTACATGATTATGCAAAATAAAGATGCAATA  
TTAAGTATGAAGGTAAAATACCACAGTGTAGGCAGCAGATGTAATCACTGAGCCTTCAGG  
TCCAGTCACCATTTGTACTTTTCATATAACTGCTTGGAAAATCTCAACCTTTTTGGGCTTA  
CAATATAATGCCATCAGTTAGAAGTCATCTTCTCCCAATGTCTTTTCATGAAGTGATG  
TAATAGGATATGCTGTGGGTAGCATAAACAAAGTCTTGATTGTCTCATCTCTTTTTCTTC  
TCCCCATAGTCCCTCTTATCACTATGCCACCTCTCCACTCTCATATACTCCTCCCAAAG  
ATGGAAAGCAGTTTCTGGGGGAGTAAAGTTTAAATAGAATGTTATGAGTATTTACATT  
CAATGAAAAGCTGTAAGCATGTTTAAATGTGAAATTTTAAAGTTCTAAGGAAGGAGCATAGG  
GTAAGGTTCTTTTTGGAAGGAGTATCTTTTCACTATCTTCAGAATAATGCCACCTATAAC  
CTATTCCTAACTATGTCTTCTACTACAGCTAAGTAGATGTATCAACTTATTCATTTGGTA  
TATTGTGAGCATTATCATTTTTTTAAATTAGTGTGTATATCAGGGGAGCCTCTGGGGAAA  
TGTAAGAAATGTGACTGATGTTAATTTTTTACTCCTGATTCTTTGAATGACAATTGTAGG  
GAGAAATGTGTTCTAGTCAGTTTAAACATTAAGTACCTAGGGAAAATGATCAATTTTCTG  
CTTCTCATATCTGCATTCAAAGATATCATATGTTTCATCTGGTATGCTTCTGTCTATCT  
GTTGTTGTCTCCATATGGAAAATAGGAAAACATCAGTCTAGCTATGCTTCTTGCTTCTTG  
TGTGCCATTAGCAAGTTATTGAACATCCAAGTCAATTTTTTTATAATTACAAATTAAAG  
ATCGATAATGACTGCATTATAGAAATAGTATCAGGATATAATGTACGTATACCTCTATA  
AAGACATATAAAGGGACACAGGCATATACATATTTTTCTTGACACATAGACATAATTA  
TGTCATTTTTATCCCTTAATTTTCATGACTGAACTTTTTGTGATGTGGTGTATAGCCAG  
CTTCTGCCTTCATGGGCCAGTCTGTATCTCTGTAGCTCTTTATGGCCTCTGCCCCAGCCT  
TTTCCTTAATTGCATATTTTCTTAAAGGTGTGAATAAAATGGTGTGGCACACATTACT  
CTCCTTTTCCACACTAGCTCCACCCACCCATCTCCTTCATACTGATTGCTTAACATTGCC  
TTCTTGCCCTTTAAATGAAAGCCATTCCCTAATATTGGAATAGTTTGTCTTCTCTCAAC  
TTAAATTTGCCTGTGCTGGGTCCCATTCAATTTAGAGTTTTTGTGTTGTTAATAGGTTGTT  
GATAGGCAGGTCTATCACTACTAGTGTTTTAAATAACACACACATTGGTAATATGTTGAT  
TTAACTCATACATTGTTAAAATACATTGTGAAGTATTCATAGTTAAAATAAATTATCCAT  
TAAGTAATTTACCTAATAACAGTTTACCCAAGTTAGGTGTGTGGAATGGGGAAATATTTG  
TAATAAGTTTGTCTTCTACAGAGTTAGTCTTGTGTGAGATATGTAAGTGGTAGAATTGCA  
AGTTTCATGTTACTCCTAAGCCTAGAGACATTTATTTCTGCTTCTCCGAATGCCCATTTT  
AGTTTCATGGGTGTTTGTAAACCCATCCTTACCTACACAGGAAGCAAAAAGGGGTTATTT  
CTAAACCTTTTTAGATATAGAAATAATACATCACTCATCTCGGCCAAGACTCAATAGAA  
TCATGAATAGTGACTGTAAAAGGTAATATTAACATTTAGGCTTTAAACCTATTGTGCATT  
TTAGTTTTAAATGCAACATGCTAATCTGAATAAGAATTAATCTGATGCCTCTACATTT  
TTGCTAAAATCATAACTGTTTAGTCTTACTTAGTAAAATAAATTATATCTTTGACTTAAA  
ATCCCAATGATAACTTTTAAAGATGGCTATTTTCATAGATAACAGCAACATTTATCATGGAC  
AGACAATAATGAGAATAACATGTGCAACTGATAATTTAAATGCAATGAGTTATTTCTGTA  
TTTGAATAAATATATTTGGGAAATGGGATAATTAATAAATACCAGTTTTCAAGAGACCAA  
ATCTAAAACCTCAAACATAAACACAATGCTCCAGTTTTTAGAAAACGTCTTGATTGTAGT  
AGTGCTACATACTAAATTGTATCATATGATTTATATTAATTTTCCTTATTTTGTATTTT

FIG. 11



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AGATTATATTTGAAAATTTTCATGTACTGCAGCTATGTTAGCATCTCAAAGTCTCCATAT  
TCTCACTCCGCTCCGAAACATCCACTGCTGATGTTATTTAACTAGTGAAAGAAGATCCTT  
CCATGTTTTCTTCTTATAGCATTCTGACATCTTCTCCACCCTAAGGAATGCTGGCTTTATT  
AAGTATGTTTCAGTCAATGACATGTGATTGGTGAAGCTGACGGTATTTGTCTTCAGTTCC  
TTTTTCCCTGCAAAGGAAATTTGTTGAATATTTATTGGGTACTATATGCCAGGTACTAT  
ATGTCAGGCTCCACTTACATATACTCTATTGATGCCTTACAACAACTTATAATGAGAAG  
ATTAATAGGTTTTACAAATAAGAAAAATGAATTCAAAGAGCAATGCTAACTTACTCAAAA  
GTTTAGTCAGGCAGTAAATAGCAGCACTAGGTTTCAAATATGGATTTAACAAATTCATG  
GTCCATGCTTATTCCATTACTTTCATCCTCTTTCCTTAGCTTCTAACCCCTGACTGGA  
GATGCATAGGCCAAAAAGAGGAAGGAAGAGATACTTAGATGTGCCCTCTAGACAATTTACA  
GAGTTGTTTGGGCATGTTGCCATGCTGTTTTCTGATAGACTACAGTTCTTCAGCTCTGA  
GGATGAGCTCATTTGATAAGCCAATCAAGGTCGGGCTAGGGTTACTTTACAAGAGAAAAT  
TTCAAGGTAATAAGGTGCTGCCAAAAATGCTTTACCTGTTCAAGGGGTTGACTCACTG  
GAAAAAAATGTTAGATAATTGTGGCCAAAGGATTATTTGTTATTGAAAGTGCTATTTTT  
AGACACAATTTGAGCCTGAGAGCCTAAACACTTAACACTTCACATAATCTACAGATATTT  
GTTTTTTTTCTTTTTGTCTATGCATTGCCAAATAAATAGTATTTATTTAAACAAATCATG  
TTGCTATTGATTTTTATTAAATAGATGAACCTTTTTTAATTTTTTTTTTTTGAGATGGAGT  
CTTGCTCTGTCAACCCAGACTGGGGTGCAGTGGCACAATCTCGTCTCACTGCTGCCTCCAC  
CTCCTGGCTTCAAGCTATTTTCCTGCCTCAGCCTCCCCAGTAGCTGGGATTACAGGCACA  
TGCCACCATGCCCAGCTATTTTTTTTTTTTTTTTGTATTTTTTAGTAGAGATGGGTTTCACC  
ATCTTGGCTAGGCTGGTCTTGAACCTTGGCCCTGTTATCTACCCACCTCAGCCTCCCAA  
AATGCTGGGATTGCAGGCATGAGCCACTGTGCCTGACGTGAACAGGTCAATTTCTATATC  
ACCGGACAGTGTTCTGGATCAGAATAATATATTATATGTATGAAGAATCATTACCTATT  
ACATCAGACATGAAATGACCTTTAGATACTGACTTTGAAAGAGTTTGAGATGCTATTGGA  
TGAAACACATGACCCATATGACCAGTCTTTGAATTGCTGACTCTGAGTATAAAATGTTT  
TCATTTACCTTTTGTTTCACAATGAGAAGTGATCTCTTAACCAAGTAAATGAATTAATCG  
ATATTTAAATAACATTAAATTTCTTGCCAGAAAACTGTTCTTTTCAAAACAAAAACA  
AATTGCTCAAAATAAATGACTATATCTTTATTTCTAAAAAATGTTTAGAGATTATTATTA  
TTGGGTCTTTACAAGTAATTTGCCTTCAATACTAAACACATGAGAACAATGTTTAATATT  
TATATAGTATTTTACTCTTCAGAAGATATTTGTCCATATTCTCTCTCAGTTATTCTTCAC  
AACACATTATGAGGTAGGTCTTTTTTAATGAAAAAACTCAAGTGCTTGAAGTGATTT  
AAAATCAGTTTGGAAGAAAAGCATGGGCATACAGAAAAGCCAAGTGGTTGTGTGTCAGCT  
TGGGAAAAGCTTGCAAATTTCTGTATTTCAAGAGGCCAGGATGAGGTGTGTAATTATCT  
TTTACTGGTCTTCAGCTATCCTGTCTTTGATATGTGATTGTGTCAAACTATGAGGAAAA  
ACTCACATTAACAACTTCATAAACTTGTTAAACATAAAATAAATTTTCGATGTTTTAA  
TTTACAGTAAGAGTTTATTCTTACAAGTCCTTAAATACCCAAAGTTCTTTCAGTTATCAT  
AGTCTTTTTCTAGTAGACAGAAATCCATGTGGACTGTTATTGTTCTGAATAGCTAGGCTAT  
GCCATAGTAGCAAAACAAACCCTGAATTTTCATTGGCTTAGTATCACGAAAGTTTATTCT  
TGCTCATTTAACATCTGAGGTGGGTGGAGAGTCTCCTTCATCCAATGACTCACAGTTCA  
GGCAGCCTCCACATTTTGTGCACTATCCCTAAAAGGTGGACTCTGTGGTAATCAGTTTCC  
AATATGGCTTCCAATGACCGCCCCCGGGCCCCGCCCCACTTCCCTGATAGTCACATCATC  
GTGTAGTCCCTTTGCATATTATGCCAGAATTGGTCTGGGTGACCAACAGCTCATAGCAGC  
AGTGAACGATGTCACTTTCAAGATTACATAACAGGAGCTTACAGCTTCTGGCTCAAGTA  
CCCCTTTCTCTCTAGCTCTTGGATCTCTTCTTCTGGAGGAAGTAAGCTGCCTTGTGGTG  
AGCAGCTGTTGGCTGGAGTTAAATCTCCAGCCAGCAGCCAGAGAGGAAATACGGTCTGT  
TAACAACCTCATGTGTGAGCTTGAAGCAAATCCTTCAGACCAGGTTGAGTCTTGAGGTG  
ACTACAACAGCCACTACCCCAACCCACCCCGAGCTTCAGTGCAACTTAGTAACAGACACT  
GAGTCAGAACTATTCAGCTAAGCTTCTTGACAGATTCCCTGACCATTACAGAAGCTATGTCA  
AATAAATTTTTGTTGTTTGACTTCAGTTTCGGGATAAGTTGTTGCACAGCCTCTAAAGTT  
GTGAAC TAGAAGAAGTATACTGGCTCTTAACCACCTTGCCAAAAATTAACACTTGTGAG  
TCATGGTCATATTCAATTTGGTCCAAATCAATCATATCGTATCAACCTAACTACAAAGGGG  
ATTGGGAGATGGTGATGTCTCTGTACAGAATCTATATAATAGTTAAAAGTATTTTTAAC  
TTGCATAGACTCAGAACAAGATAATTTGGAGGAATTCATGCTTAATGGCATACCACTAA  
GATAAGCTGATAGATATATCGTTGCGATTTGGGTCTCTGACAATAGAGGCAATTGATAAT  
ATTAAGAGACTATGTGCCAATTATTGTGCTTGGATTGAGGGTACAAAGGTAATAGAACCC  
AAGGAACCTGCATCTTTTTTGAAGATAGACACATAAACACATACTTTTTAAATAACGTG  
GTAAGTGCTACTATGACAGATGGTTGCACAGAATGTAGTGGAAGTATTTGAGAAGGACAC

FIG. 1J



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TTAGCTCTGCTGGGGGATTAGAGAGAGATACAGGAGGAGATGACACCTAAACTGAGTTTT  
AATAGATGAATTCAAGTTACCCAGGTGAAGAAAATTGGGTAAGGATGTTCTAAGCAGAGG  
AAACAACATAAGCAAAATCAAAGAGGCGTGAAATAGAATGAGCTATGAAGAAAGTGTTAG  
GCAATTGGGTAAGTCCAATGTAAGTGCAGATGAGGAGAGTCTGGAAATGAGGCTGAAGCA  
GTAAATAAGGATTGGCCATAAAAGACCTTGTGTACAATTCTTAAGATCTAGGCTTTGACA  
CTGTTGTTTAGGGGGAGCTGTTAAAGGATTTTAAATTAGAGTACCATCATTGGTTTGCAT  
TTTCCATGAGAGCATTTTGAGGAAAATGCAGAGAATAAATACATGAGGGGAAAGACTAGT  
GAAGGTTTTACACTGGGGTTTGCATCCTGTTTTGGCAATAAGCTTGTTTTAATGAAAAC  
AAACAACAAACTGACAATAAAGAACATAATCCAAATTCTCCAGATAATTACTTCCAGGA  
GGCTTTCTACGTGCTGCATACAAAACAAAGAAAGAAAAACATAAAGTGAGAAAACGAAGG  
AAAAACAAGGAAAGAGAGAAAGAAAGAAATACATATTGGA AAAACTGTTGCTGTTTTTGT  
TTTGCTGAATATTTAAATTTGAGAAGCAATTTCTCTTTTTCTTTTTACTTTTTTTTTGA  
GATAAAGTCTCACTCTGTTGCCAGGCTGGAGTGCAGTGGCGCCATTTACAGCTCACTGCA  
ACCTCCGCCTTCCAGGTCCAGTGATTCTCCTGCCTCAGCCTCCCCAGTAGCTGGGACTT  
CAGACATGCACCATCACGAGCAGCTAATTTTTTGAATTTCTTAGTAGAGATGGGATTTTAC  
CGTGTGCTCAGACTGATCTTTAACTCCTGAGCACAGGCAATCCGCCCACCTTGGCCTCC  
CAAAGTGCTAGGATTACAGGCGAGGCCACTGCACCCAGGCGCAGGTTTTCTTTATGATG  
TTTTAATTATATCTTTCTTGGAACATATATGTATGAATCTTGCATGCCATAGGTCTATTA  
ATATTTTCCAATATTCTACATGGTTTTTTACTAAAATCATTTTTATGATTAGTTACTGAC  
TGAGGTTTCAATGCATCACTGTACTCTAGCTATCTCTCATTTTAGCTTTTACATCACAT  
TTTGGCCTCACACTGAAACACAAAATATTA AAAATTTGAGATCTAATAAACAAATTTTAC  
ATTTTCCAATAAATCCCCACTTCTTTCTAAATTTTCTACAACCTTTCTAAACATTCTCAC  
TTGAAAATTTATTTTAAATGACATGTATTTTATTTCAAACAATCAATGAAGATGCTACATT  
GACCCCAAGTGAGCCCTTAGGGAATTTCCGTGAATATTTCCCTACAGGTTGGCATGGTAA  
CACACTTCACAATTTCTAAATCTGTGGATAGTTTAGAAGCTTTTATTTGCTGTTCTTAGT  
TCACAATGGAATAACAACATGATTAAAAATTATAATATCCTTTGTAGATTCTTAGCTT  
TTATTCCTACTCAGTGACTCTAAAATGAATTTATAAGGCCCATGGTTTATAACCATGTGA  
GGCCTTGATTTGTCTACTACATTGCTAGAAATGGGGTCAGAAGGCCACCAGCTTTAATAA  
TTTAATTCATCAATTCGGAATGAATTTGATGAGTCAACCACTTTGGTAGAGAACCATATT  
GCTCATAAATACTGTTTTGAAGGCAATTCGTCTTTTCAAAAATGTGAAGATTGTGCTGAT  
CTTTCTGGGCAGGGTTATGGAGGTGTGATTAAATGCTTAAGAAACCATTTTGTATTATA  
TTAAACCGAATCAACTTTTTATTATTA AAAATAGATAAAAACCTTAGCATCCTCAATTATA  
ATACTTTATACAAAAGTTTCCCAATTTTATATAGACTGAAGATAAAAATACATTAACAAA  
TCTTACCAGTGGTTTTCAGGAAAATAACTTCATAATTATTGAGACATTTATGTGTTTGGGC  
TTGATTTATACTTTGGACACAGGAAAACCTAGAGAGATCTGGTTCTTTGAAATCATCAGA  
GATGGTGATGGTGACTCAGAGATTCTGAAAATCAGTAAGATTACCCTAGTTTATAGACG  
TATGTGTTATTTTTTCCCCAGGCATAATGAACCTTTATAACTTGTCAATTGACAAGAAGCC  
AAATCATCTTAGAGAAAAGGGGGAGAATAAAAATTTAAGAACTTAAAAACACATAAATAA  
AAACATGTACATACCTCACACATGTGTACACACACAGTTTTGGGGATTGGATGATATGAAT  
AATAAATTAATAACACCTAATTTTTTCATGCAGGATTAAGAAAGTATCTTCCAAACATTA  
AAAATGCTGAAAACCTGGACATAAGGCCTTGAGTTTCCCAAATTCAGGACATATTTTCAAC  
TATCCCCTGAGTAAATGAACATAACATTTACAGAAGTAAAAATGATAAATACACTAAAG  
ATGAATAAGTCCTTGAATTAACAGCCAAACAAGAAGGCGCATCCTTTGGATGATTGATCA  
CTGTAGCATGATTTCTTTTCTTGAATAGACAATATTCCTTGACAATCTTTCTGTAAACA  
GAATACAATGTTTCCCTAAGCAATATATGCGTGCTCTAGAGTTTTTACAATTTCTGATCC  
TCCTATGACTGGCTCCTGCTCAGCTCACACTGCATTTTCTGGAAGTTCTCTTAGAATGC  
CAGCTTTGAATCACTGCTCCCTCATGTGCTGTGTGTGATAGCATCCCATTTTAGTTTTGT  
CATAGAATTGATTACCATTTCAAATTTGAATTTGTTAATTTATTGTTTCAATTTTTCTGTTGTC  
TCCCTTAAGTAAAAGGTAAGCTGCATGAGAATAGTTTCAATTTTTTTTTCTGTTTGCCAAT  
GTATCCTCAGTGCCGAGAACAGGTTTCAAGGAATACAGAATTTTTTAGTTAGCAAATGAATTA  
AAGTGTAAGACTTCCAGCAGGAGGAATTTTTTACATATAAGTACATTTTTTAAATTAAGC  
ATTGCAGGCTTTAAATTTCTTCTATATAAATATTTAAATAAAGCTTCAATAATTTGAAT  
TGCTTTTGTGATTATTTTGTGTTTTATACCTTGAGTAACCTTATACATCAACTATTTTGTAGT  
TATTCTAGTAATGATTATGAAAGACCATTTGAAAATCTTTCCCCAGCACTGAGATCTCCT  
TGACATGACTAAGTGATTATATCTATGCAATTATATTGCTCTTCTCAAGAAAAGCAAAT  
GAAATTTACAAATTTGGTAGCTTTTGTGTTCTTTGTTTTCTCAAGTAAGATACACCAAGA  
TTCTTTTAAATGATACGCTATATTTCTGCAATAACTGAGAAGAACATGTAATGTGCAAAA

FIG. 1K

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CTCTTAAACTCTTTTTGTTTCAAAATAATTCTTGTTGTTTTATATAAAGTCTAAGCAAA  
TACTTAACTGAGTGTGTCCTCAATGAGGTGAAACAGCTGTGACAGAATGTTACTATGACT  
CTGTACTTTCTATAATAAAAAGGGACAGACATATCCTCACCTGAGCCTTGGGATGTTTCA  
GGCATGCCCATAGAGCCTAAGCTTTAGGAATCCTCTGTCACTTTTCCATTGCCAGTGA  
CTTGTGCCAATTCTAGGGTTCTGGACTGTGCAACAATGGAAAAATAATAACACTTTTCA  
GGTGGCGCACAAAACCAATGTTTCATAGTAGATGGATAGTTCTAGACACTTTATTTAATAG  
AGAATAGGAGAAACACTAATCCCATCTAATTCTGCCTTCAAACCTCCTAAAAATATTCATCA  
TTATGAATTAATAAAAAAAAAATCAAAGTGTAACCTCACCCAGAGAAAGAAGACATTGGGGC  
CAGGTCTGGTGGCTCATGCCTGTAATCCCAGCACTTTGGGATGCTGAGGCGGTGGATCA  
TGAGTTCAAGAGATCGAGACCATCCTGGCCAACATGGTAAAACCCCATCTCTACTAAAAA  
ACAAACAACAAAAAATTAGCTGGGCTTGGTGGCATGCGCCTGTAGTCCCAGCTACTTGG  
GAAGCTGAGGCGAGGAGAACTCACTCAACCCGGGAGACGGAGGTTGCAGTGAGCCAAGATG  
AAGCCACTGCACCTCTGGCCTGGTGACAGAGTGAGACTCCGTCTCAAAAAAAAAAAAAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAAGGAAAAACGAAAAGAAAAGAAAGCAGATATTGGTAATTCT  
AGCAGATCCTGGAAACAACTGAACCAAAATTTATTAATATGTATTATTACTGAAAAATCAGTA  
ATGAACAAAAATTTACAGAATGGGCTTCTTGAGTGTGTACATTTCCCTTATTACATAACT  
CTTCAATAAAAGTGTGTGTACATCTTTTGTAGTTAATTTCTACAACAACTAGTGTGATAG  
GGTATTTATTTGATCTTTTTTTTTTTTTTTTTTTTTTTTTTACAGGTAGTGACATTCAGTATTA  
GACAGCTGCTATTGTGTAGTTGTCTGAATACCTTTACATATTATCAACTGGCCTTTTCA  
TTCTGAGTTGTGAGTAAATGCTCTGTCTCCAGACTGGAGTGCAGTGGCGCAATCTCGC  
CTCAGTGCAAGCTCCGCTCCCGGGTTCACACCATTCTCCAGCCTCAGCCTCCCGAGTAG  
CTGGGACTACAGGCGCACGCCACCATGCCCGGCTAATTTTTTTTTTCTTGTATTTTTAGTA  
GAGACAGTTTTCACCATGTTAGCCAGGATGGTCTTGATCTCCTGACCTCGTGATCCACC  
CGCCTCAGCCTCCCAAGTGCTGGGATTACAGGCATGAGCCACCACACCCGGCCATAAAT  
GCAGTCTTGTTTCCCCACTTCCATTCTCCTTTGACAGTACAGCTATGCTAGTCTGCGT  
AGCAAAATTGAAAAAATATGACCTGTGGGATTTAAACAAAACACAGTGTACACACATTTT  
CTGGTAAACTTAACCAAAAGGGACTTGGGTTCCATAACTAATCACCATGCCTCAGTGAT  
CTGTAACCTCCTTGAGGTACCTGATCACAGTTACTAAAGGGAAAGAGGAGCGAGGAATAC  
AAGAGCAAAGTCAAGCCAGACATAGATTTTATCTCTTTGTAAACAGGAGTTTCAAGAGACC  
GCTCTGAATGCTGAGTTAGCATCAGCAATAATAGAAATATATGCAGATTGTTGATTTGAA  
GTCATGCAAAGATATCTTTTTCATCCAAATGGAGGCAAAAGCATCATAGAGCACCAGAGG  
GCTAAATCCAAGTGTAGCAGCAAAAGGTACACAGAAAAATAAAGCATCCTGAACCAACGC  
ACTGACTTTCTAGGGCTTATCTAATTTGGAGCTATTTCTTTTCTTATTTTCATTTCAGCAA  
ATATTTATTGAACACCCACAATGTGTAATCTGTTCTATTACATTCTGTGGAGGAAATACA  
GAAGTGAATGAGGCATGGTTCTTACCTACAAGGAATTTCTAATCTTGTGGGGGAGACTAA  
CATGTAAACAATAAACTATAGTATGAGGATTACTGAAGAGGCATATGCTAAGTCTCAGAA  
CATTGAAATATAAGAGTTGGGTTTGACATGGGGAAAGAAATACCTTCTTCACTGAGGAGG  
TAGCATTTTGTAGTTATTGTTGACATGTGAATACGATTTTGAAAAGTTCCAAAGAATGAAA  
AATTCCACCTACATTGGTGAAGTACTAAGATTAAATGCATGATAGCTTGAAGACACAAAA  
ATAATTATTTATAAACCATTCCAAAAATCATTCAGGGAATTCCAATAATACACAAGTTTT  
TAAACACATTTCTGGGTAATTTTGAGTAATAAGGTCTTAATCTCCTCTACTGCTTTCAAT  
TGTTTTTGTGGCCTTCTTTATTTTGTGGGTATCTGGCCAGTCTTGTCTGTAGTGTATTA  
TGGTGGATTGGATTAAACATGTTTTGCAATCTCTGGAGTGATTTTAAAATGACTTGTGTT  
ATATCAGAGTTTCTTAAAGGGAGATTAATTTGGCTTAATGGTAAGAACGGATTAAAGTTA  
TGAGATACCAGACACTGGGAAAACAGTTAGAAGCCTGTTGAGACTCTTCAGGGCAGTTGT  
TGTGAGAATGAAGTTAAGACAATGGGATAGAATATGAAAAAAATGAAACAAACATGAGA  
GGCAGTCTGAAGATGGAAGTTGGCAACTCATCAAATGTGAGAAATTTATAGGAACAGAAA  
AGAACCTGCTGATTAATATAAATTTTCTGCCAAAGAAAGTACAGTGGCTCTCCTCAGCAA  
ACTAACATGGGAACATAAACTAAACACTGCATGTTCTCACTTATAAGCAGAGCTGAACA  
ATGGGAACACATGGACACAGGGAGTGGGACATCACACACTGGGGCCTGTTGTCGGGACTA  
TGGGAGGGAGACCATCAGGATAAATAGCTAAAGCATGTGGGACTTAATACCTAGGTGATG  
GGTTGATAGGTGTAGCAAACTATGATGACACACGTTTACCTATGTAACAAACCTGCACGT  
CCTGCACATGTATCCCGAACTTAAATTAATTAATTAATAAAGAAAAAGACAG  
TGCTTGTCTTATTCGTTTTTTTCTTAAATGGGAAATATGTAATATATATCAACTGTAGT  
GTATAGAAGGGTCATGATGAATTGGACAAAGATACGTGGAGTTTGAATTGCTAGAGGAGT  
ACCCACGTGCAGTTTCCAGCAGAAATCAGGGCTTGTTCCTCAACATGCTATTCACAATC  
AGTCTACTACTCTCAGGTATTTGTTTTTCTGTGTGGCTATGCAAGCAATAGATACAGTTT

FIG. 1L

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ATGTGAAAATGTTTTAGAAAATGTCTTCTGGAATAATTAAAAGCATACAAGGGAATGTAA  
ATCTCTTAATGTGACAAGACCTTTTTGCCACAATAAACAAATTCATTAGTTCAAAAATA  
TTTATTGTGTGCTTATTGCAGCAAACAAAACAGACGAAGCTCCTTCTTGTAGGGAACCTTA  
TACTCTAGTGATATTTAGTATATATTTTGACAATTGAACCAACAGGATTTGCTGACGGAT  
TGCCTTATGGGTATAAGAGAAAGAGAGGAGTCCACACTTTCATGCCAGGTAGGTTGATGG  
AGGTGCCATTTACTGAGATACAGGGCCGTAGAGGAGGAGTGTGTTTGCAGCAGGGAAGGA  
GAAGACTCAAAATTTGGTTTTGATCATACTAAATTTGATATAGTACAGGTAAGTGTATGG  
TGGCCATTAGAACATGAAGGTAAGAGTTTAGATAAGGAGACAGGTATGGTGAATACATC  
CAATATTTATAACCAATATTATCTTTTGTGTCTGTACCTTTTATACATTCCCATATAT  
ATCAAAGACTATAGAAGGGACTGGATAGTGAATAAGTGATTATACATAAATCTTTTTTA  
CAGATTATTTTGCTCTTGATTTCTCCTATGTAAATCATCACAGCTACATTTTTTAAATC  
TTAAAAAGGATTACTTTGAACAATGCATTTAAACATCCAGAAAACAAAACAGGAGTGCA  
TGGTAAAAATCTGATTTTCAAGCGTATGCCTGACTTATCAAGTCAGAATTTTCAAGGAGT  
GAAGACCTTGGAACTTACACTTTAAATAGAGCCTCAGTTCACCAAGTATGAGAAGTCTCTG  
TAACAGGGAAGTAACCTCCTGTTATATTTGATGGAGGCCAATTGACAAGCCAAGTAGT  
TTTCCATTTGACAAAATCTATTGTACCAATGAAGAGCTATCAGAGGGGAGTAGATTAA  
AACACCTCCCTTGAAATGGAATTTGGCAAGAAAGCAAGAAATTACAGCAAAAAGACCAAT  
AAGAGGAATTAGGGGCAATGAAGGAAGGAGCAAGATGTGGGAACCCAAAAGTTTTCT  
AGTAACAACCTTGAAATTATATTTTAGTATATTAATTTAAAGTAGAGTTATTAGTGCA  
TACATTGGTGTAAATTTATTATTATTAAGCCAACAATATACTTTTAACTTATACAACCT  
TTGCAAAAAGTACAAATCAGAAGTCTGGGCTAAGTAGAATGCATAATAGAATCAGTAGT  
GCAAAATATTGTTCTATATTTTCTAGCTTATGATTTTCTATATAAAGTCAGTCTTTCAGG  
ATTAAATGAATGTCACCTTCTTTTACCATGTGTCTTTAAATTATTAAATCTATACAC  
ATATTGCTATACATAGTAAATATAGTTAGTCAATTATGTCATGGAAAGAATTGAAGGGTT  
GTTATAAATTTAAAGGTGTTTCACTATACAAAACATTTGTGAAATACTGGTGCTGATTTA  
GTTCTAGTATCTCTGATATATTAATCATAAATGTCAGGAGTTATTGGTCACAAAATAAA  
CACCAGAATTATATGACAGTCTAAAAACAAAACAAAAAACTTCAGCAACAATATTGAAG  
ATATGGAAGTGCCAGAAGAATAAGGATTAAGACAATGAATAAAAATCTCTTCCAAGGACT  
GGTCTACACTAAGAGTTTAGAAATGCATTTTTTTTTTTCACAGAAATATCCTTAATCCTCTA  
TATAGAAATGAGAAGAAAACATAAGACTTTAGCAAGCTCCATCTAATCCATTTGCAGACA  
TATGGTTACCTATCTTTTCTTCAATATATTGGAGTTTGCAAATATTCTACCTTCAAAGAA  
TAGGTGTTTACCAAAACATTGTCTGCAAGATTTCTAAGATTTGAAATATATTTGCTATAGT  
AGGTTAGAGATGAGACATTTTACTTTAAATTGCAATAATTCAGACTTAAAATATAAAAT  
GTGTAAGTCTAAATTTTTTTTCTATTTCATTGCAAATATATCTTATATATACATAAAATCC  
TGTGTATACTCATATGAACCTTTAAGGAAATATCAGAGGCATCAGTAATAGATAACTTGCA  
TCTCTTTTACATTCAAGTCTCAAGCTACTCAAATTTTAAATCTTTTGTTTTTCAATCCAACAAA  
AAAAATTAGGATCTGCCTTGGCTTTTGCTAAGAAAGTAATTATTGGCTGGACATGGTGGC  
TCACATCTGTAATCCCAGTACTTTGGGAAGCTGAGGTGGACAGATTGCTTGAGCTCAGGA  
GTTCAAGACTATCCTGGGTAACATGGTGAGAACCTTTCTCTAAACACACACACACGCGCA  
CGCGCGCACACACACACACACACACACACACACAAATTAGCTGGGAATGATTACACGC  
CTGTGGTCCCAGATACTTTGGGAGGCTGAGGTGGGAAAATCACCTGAGCCCAGGAAGTCGA  
GGCTACAGTGAGCCGTGATTCCACCACTGCACTGCAGCCTGGGTGACAAAAGAAAGTCA  
TTATCTTCAACACTGTGCATACACACTTTTCTGCATCTAGATCCCAAATTTTTGTTTTGT  
ATTTACATAGAACATTGATAAGTAAGGTAAGTATTAATTGATAAAACATTTCAAACCTCAT  
TTTTCACTAAATCCAATGGCCTTCTCTTTTGCATGAAGTCTCTAAGAATCATGTTAATC  
TACATACTCAATCTACGTAACAACCTGGATATATCCTGTAGTTGTTGCCATTTTTCTGCT  
AAATGTTATCTTTAGCACTAAGCATGAGTATGAGGAAACAGTATCTGTGCTCAGATTCCA  
GAAATGAAGAAAATGTACTGGAGGTCTTTTGGATAATGGCTACAAGGTCACAGGGACTGA  
CTCCTTTGGAAGCTCAGCGATAACCATTTTCAAGAGAAATATGTCAACATCTTTCAGTCT  
AGAACCTTGATGTTCTGCTGAGATCTAATCTGGGGGTGTCTACTATTGAATAGGTATAAA  
CTAAATAAAAATAGTGAGAGAACATTCATGTGTTCACTCATTCCTTCATCAAACAA  
ATATTGAAAGTCTATTAATTGGCAAGCACTCTTCTGACATTAGAAGGAGCAAAGATAAAA  
AAGATATTATCATTAACCTCAAGGACATGACAGCATCATGGGAAGGCCAGAAATGCAATA  
TGTTAAAGTAAAACACAGTGTAGTGTCTACTACTAAAGAGATATAAACAGAGTACTGTGG  
TCTAAATCATATATATAACATTTGCTTAATGGATGAGAAGGAACTTTAACTTCAGGAG  
GCAGAGCATTAAGAAAGTGAATGACAGGAGGTCAAAAGAAAAGCCGACAGTGTTCAG  
AGGCAGGGCATAAAGGAGCTAAACCTTTGCTACCTTCAGTTTTTTATTATCCACAGAACGA

FIG. 1M

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CAAAGAAACAACAACAACAACAACTTTGGATTTGAGGGTTTTTGTTTTTCTTTTTT  
TTTTTTTCTCTCATTCCAAGCATCAAACCTTGGGATTTATTTACCTTCTAGCAAACCAA  
AATTTATGGGGGCATTCTATGGTCCCTCACCTCACCCCATTTTTCTGTTTTACCTATGAA  
ACTTGATCAAAATACTGTCTCCACATTTCTCATAAAATACATTAGTTTAAATTTCTACTA  
TTACTTTCTTTTAGTTGATTTAAAAAAGGTCATTTATGACCTATTTAGGTTAGCATCAT  
TAATTTTATCAATGTAAGAATATGGTAGTACAGTGTGAATTCCATTAATGGATATGTTGA  
TACCATGGGTTTTCTCTGACCTTTTCTCTCCGCTCCTCCCTGATGATTGGTTCTGAGCTT  
ATTATCATGTCTAGCAATGAAACAGAAAAGGGAGAAAAATCTCAAGTAGGTTGTCTGTCTC  
TTTAACACTGAATAAAGATTTTTTTTTTCTCTAACAGACTTAAAAATAGTGCCCTAAAAAT  
GTTTTGTTTCATTTGTCTGAATTCCCATTCTTTCCCGTGATCATAGATAGTTGAGCTAAA  
AAAAGAAAAACAACAAAAACAATAAACATTGTGTCTACATTTGTATTAACTTTCTTA  
GGAATGAGAAGTAGAATCTTAAAAACCTTAGAATGGGAGTTTCCAAGCTAGCTTGCAGGC  
TTGAGTTTTATTGATAATACCTTTAGGATGCATGTATTATTAGAAACATCAGTTATTTAC  
AAGTTCACCTATTTAAAGTCTAATAGGAAAAATATTTTCATGTTGCTAAGTATGTGACT  
TCCCTTTAAAAAGATAAATAATGCTTTCCCTTTAAACAACAATAGTAAAAGAAGTAGAGTTT  
CTTTTAAACACATACTTTTATATTATAACCCATTCTGTTTAAAAAATAGCAGGCATATAA  
TCTAGAAATGCAATAATTTAGTGAAATTTTTAAATTTATTTCTACATATAATTAATATG  
GATATTCGTTTTCAAATATCAAATAATAAATATGTCTGAGATGCTGACTAATCCTTAAT  
TATAGGTGTGATTTCTACTTCACCATCAATACTATGGTACTCCAAATCTTAACATGAGTC  
TGATTTTCTAATAAACATGATGAAAAAGTTATGAAAAATTTTGAGATTTACTTTGGGA  
GGTTCATTGTGTCTGTTTCAGCTTCATAAATATTCAGTTTCTATGAGTTTGGTATTTAAT  
TATGTGTGTTTGTCTTCAGTAGGCTGGAAGTATGACCATTGGGAGATCAAACGATAAG  
ACATTAATGACAGTGCTTTTACTGAATCTAGTACTTTTTTAAATGAAAGAGATGTTGG  
CCTCTTGTTATGTTATAAAACAACAATTTTATGGCTTTAAATTAAGTACAATCATAA  
CAGAAGACAAAATTAGATTAAAAACAACATGGAGTGACTCATATAAAATATTTAGAAA  
CCAATAATACAGATAGAGACACATTAGTTCCCTCTAGACATTGTGTTTTCCAGTAAATGA  
TCACCAAACCTTACCAGGAAAATGATAATTATCAGATTATTTACTTTCAGAATTAAGGCA  
GGAAGAGAAAAAATGAATGAAGAGGAAACACAGTAACCATATAGGACAATAAGAGTGAA  
TGAAGATAAAATGAAAAATCAATAAGATATCGACTTTCTTAAAAGACAAATATCACAATA  
GGAAACACCTCAGAAAGGGAAATCTCAAGAAAATAATAAACTGAAAGAAGAAAACATATC  
AAAACAACCTTGAGGACTGACAAAGTTTTAAATGTATTTAGATAAAGATACCATGAGGAA  
AGTGATCAAGGTGTTCTAGGTAATCACTGAAGATAAACTAAAAATAGCTTAAATTAATA  
TCAGATAGAGAGAAGGTAAGTGAACAGGCATAGAAAAGAAAGTAAGAAGGAATACAATCC  
TGAACATCTTAACAATGTCTCAAATGTCTCAGGAATTGATCCAGTTTTTGGCTGCACAACAG  
AGTGGCTATAGTTAACAATAATTCAGTGTATTTCAAATAACTCAAAGAGTAGAATCG  
GAATGTTGCTAACACAAAGAAATGATAAATCTTGAGGAAATGGATATCCCAATTACCT  
GATTTGATCTTTACACATTGTATGCTTATATAAAAAACAGTATTCATGGCCGGGCGTGGTG  
GCTCACACCTGATTAAGCCTGCCTTTGGGAGGTCGAGGTGGGCGGATCACAAGATCAGGA  
GATTGAGACCATCCTGTGAATGGTGAAACCCCGTCTCTACTAAAAATACAAAAATTAGC  
CGGGTGTGGTGGTGGGCGCTGTAGTCCCAGCTACTGGGGAGGCTGAGGTGGGAGAATGG  
CATGAACCCAGGAGGCAGAGCTTGCTTGACAGTGAGCTGTGATTGCACCCTGCACTCCAG  
CCTGGGCGACAGAGCGAGACTTCGTCTCAATAAAACAACAACAACAACAACAACAAAAAC  
AAAAACAGTATTCATAATAATTAATAAATTAATTTTTTAAAAATAAAATAAATATCAGTA  
ATTTAAATTTTTCCCTATAGCATAGAGATCTGTAATTAATACTTGTGATCATTTGTTGTTT  
CTGTCTTCCCAACAACACTACACTCCTGTTTCTTCACATTCCCCCTTCTTCTAACAGCACTA  
CATCTTTCTTTAGGAACTATCCTTTTGCCATTTTCATGTATATGGTGGGGTGGGGGAGTT  
ATCAATCACAGTACCCAGCAGATGGGACCAGAGGCAAAAATGCCTGACCTTCTCCCATC  
CCCCAACACAGCAGCAATGAATTATAATTTGATGCACAAGGAAGTATCGGAGCTTTTG  
TGTTGGGTTTTACATATCACCTGTGGGAGATAAATGAACCTTTCCCCACCTAACCTTTAG  
CCACTTGGGATGATTAGACATAGAGGTGCCTAAGATCTTTCCCTTTGCCACATTAACAAAC  
AAATCATCTATGGCAGCAGCATAACAAGACCAGCTTTCAGAGACACAAAATGATGGAGAGA  
ACCATGATACTAGTTTTAGACCTAGTCACTGAGACTTTCTCTGCTCCTTCCCAGTTACCT  
GAGCTTTATTTTGTGTTACATTTATCAGATTTGAATGGCTGTACTTCAAAGTACTGATTAA  
AATAGGAACCAACCTATATGATTCAGGTGGTGAGAAGGAAGAAAAAGAGAGAAAATGAGG  
TTAACAAAAGAGAATAAAGAAAAAGAAAGAAAGAAACAAGAAACTCTGACTACCTCTCC  
TCTTGACATAGTTTACACTTCTGACAGATTGTTCTTCTCTAAATTTATGTAGAGATTAG  
AGTGAGGATGATGTATGCACTGTAGCATGGGTGGTCTTCCAGGAAGCCTTGACTGAATGA

FIG. 1N

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GGCAAGGAGTATGTTGCTCCCTCAGTAACCTCAAATTTACCTGCAAGCCTGATAAAAATC  
TAACACTAACACTAAACCCAATCTTATCTACAGCCCTAACTGCACCCTAATATTAACAAC  
CCTACCTCTGTACTTCAAACTAAACTAATTTCTGATTTTACTCCCATCTGCCCCTTTTA  
CCCTAAAACCAACTGTAAACTAAATTTAACTCTAAACGTAATCCTAAAACCTAAGAATTA  
ACTAACAAATTTTATCTCTATACCCAAGCTGTTAACCCCAAGCCTAACTCTAATCCTATCTC  
TAACCTAACATTAACCACAAACCTACTTCTAACTCTAATCCTAACCTAACCTCAAATCT  
AACTCTGATTCCAATTGTAATCTAAACACCAACCCACCCCTACCCTTTTATCCCAAATCC  
ATCTGAAACCCCTCATCAGAACACAAATTTCCAATTCTACTTCCCACCCTGACTCTGACTCT  
AAACATAGGCCCAAATATAACTCTAACTCGAAGTCAAAAACCTTAACAAACCTTATCTTGA  
AACTCAACCTTTTACTAACCCTCAATTCTATCTGTAATCCTAACCTAATATTATCATCA  
AACCTATGTCTAACACGACCTCCAACCCAAAACCAAACTAACCTCAGACCTAACTCTAC  
ATCTAATTATAACCCAAACCCAGGCTGCTACTTACCATAACCCCTGAAACTAAGCTTGAT  
CCTTTCTCTTTTTTTTGGAGTGGAGTCTCGCTCTGTCTCCAGGTTGAAGTGCAGTGGCG  
TGATCTCGGCTCACTGCAAGCTCTGCCTCTCAGGTTCTATGCCATTCTCCTGCCTCAGCCT  
CCCGAGTAGCTGGGACTACAGGTGCCCGCCACCATGCCCTAATTTGTTGTATTTTTG  
GCAGAGATGGGGTTTACCCTGTTAGCAAGGATGGTCTCAATCCCCTGACCTTGTGATCT  
GCCTGCCTCGGCCTCCCAAAGTGTGGGATTACAGGCATGAGCCACCACGCCAGCCGAC  
CCTTTCTCTTAACCTACACTAACACTAACTGTAAACCTAGCTGTAACCTCTAATTGTAAAC  
CTAACCTGATTACTACTACAAAGGTCCCTCTAATTTCTAACAAAGAACTCAATCCTATCT  
CAATTCACCCAAACCCAAAAGTAAATCTAAACCTAAACATAACTCAAAATGTATCTCAA  
ACCTTAACCTTACGAAACTACATGTAGCACTAATGTAAACCTAAGCCCAATCCTATCAG  
TAACACTAATGCTAAAACAAACCCCAATCTGTATCTCTACCCCATCACTGACACTACCCA  
AATCCCAATATTTAATGCTAATCATTAAGTCTCAAACCTAACTCCAACTTATCTTTAACT  
ATATCTCCAACCCCTAACCTAACATTAACCCCAAACTTATCATTAATCATACATCTAGCT  
CTAAACCTAACCCCAACTTTAACTCTTACCCTAGCTCTAAATTAACCCCAACACTATCT  
CAAACGTAAATCCTAATGCTAACGTTACGCTACTTTTAAACCTCACCTACACAAAATC  
CTGCACCTAAACTCAACCCCTAACTTTAAACCTACCTCTAATCCAAACACTAAATTTAAAT  
CTGGATCACGACTTGGGCATACTAGCACCCACTAGTGTTCTGGGTGTCATTTCTTTGCTT  
CACTCTCATCCAGCTTTCTTTACTAATTTTGGATAATGAATCAGAAAATAGTGGTGTGGA  
ATCAGGGTCTTTGAATTATTGTATTATCCAGAGTTTGTCTGCTGCAAATGATAAAACAC  
TGAAAATTAGCTTAACAAGGAAAAAATAAAAAATGTGTGTGCAGGGGAGAAGTAGGAGAG  
TTATTGGCTCAAGGAACAGAAGAATTCAGTACTGAGTTTCACAAATACCTGGATTCCCTA  
GTCCCATACTGCCATCAGGATCCAATCTGTCACTCACTCCAATCTCTTCTCCTCCCTG  
TTGGATTCAATTGTTAGGTTTCTGTGGCAAGATGAAATGGCCTCAGGCCTGTAACACAAT  
AGGATCAATTACAACAGAAGATAGTATTTCTGTTTTCTGGTTGCTCAAGCCTAAATTC  
AAGATTAGTTTATATCAAACCTAGTTAGTTTTGCTCATGTAAGGGATTACTGCAACTGGG  
TACATAATATGAAGAGTGGGAGAGTTGGTTAAGGGGGTTCTCTGAAAGGAGAATTAGGT  
TACTGTTAATGGGAGAATGAGAAATGGGTATTGTAATGACAAAAACACACACGACTACCA  
CAAATGTTGAGGAAGAATTTTCTTTTATGATCATCTAGCCCAACTTTTTAATTTCTAATT  
TTGTGGTTTTTGACAGTTTTTTGTTTTTTTTTTTAAATGCAGCATGTCATAAAGTTGGGAA  
TACTTCACATTTTTGTCTTTGAAAATTTGGAGAGTACTTAAAAAGATTTACAAAGGGGAGG  
ATTGAATTATTTTAGGAATGTAAATGGTGGTCTTCTGTCTCAGGCAATGTAGATGCTTGC  
TAGAAAACAGCTGACTCATGACTGTTTTCTTTCTAATTCATTAATATGAATTATTTCAA  
CTGCAAAGTTATCTCCTTTCTTCTCCTAATCTATCCACTTAGAGTATACATGTTCAAATT  
AATGTATTGAACTAATTTTTCTAGTAATACATTCTATGCATTACAAAAATAGCAGTGGGA  
AGGTGAAAACAAATGCAGTTATGCATTTATCTCTAAATGTGTTCAACATCTCTTATGCG  
TACTTCAAATAATTACATTTGTTTAAATTTGAAAAAATATTAACAAGAAGTTGTAATT  
TGGGGAAAATTTAAAGCTGGCGAAAAGGCTTCATCATAATTGACAATATGGGAAAATAC  
TGATTTAAATCCTAGGTTTCTCCCTTGTGTCATGAAGGAAATGAAAAATATATAAGGG  
AAGGATTTAATCAGTCAGGCAAAAATCTAAATTCATCACAGGTTTATTCACTGCATACTA  
TCAATGTGCCAGTACCTGAATGAATATATTAAAGAAATCCACCTCTTGTACAATGAATG  
TAAATGAGCAGAGTGTGGTGATTAAAGGTTGGTATTGGTGTGGGTAGACCCAGCTTTG  
CCACTTACTGCCCAAGTAAATATTGCCATCCATCAGATATCTCCACCTATCAGACCCACC  
CTGTTGTAATAACAAGATTAAATCTGTATCACTAAAACCTTTAAAAGAATTTATAGCCGA  
ATCTAGAAATCTTTCACTATAATTTATCTTTCTTAAATGTCGTTTTTTTTTTCAATTTT  
ACTATATATGTTTTTGTACTTGTGTTGCTGCTTGTGTGTGTGTGTGTGTGTGTGTGTG  
TGTGTGTGTTTTTGAACGGAGTCTTGCTCTGTGCGCTAGGCTGGAGTGCAATGGTGGGA

FIG. 10

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TCTTGGCTCACTGCAACTCCCGCCTCCTGGGTTACGTGATTCTCCTGCCTCAGCCTCCT  
GAGCAACTGGGAGTACAGGCGCACACCACCACACCCAGCTAATTTTTTGTATTTTTAGTA  
GAGATGGGGTTTCACTATGTTGGCCAGACTGGTGTTTTTTGAAGACTTTTCTGATT  
CAGAAGGTGGGACTCACAATTGTAATTCTGCTAATGGTTGTCTTTCAGTCTATCAATTGC  
TTCATAAATGCATCCACTGTTCTTCTTCTTCTGCCCTGCTTATAATTTTCCATGAGTCC  
ATATATCTTTTTTACACTGTCTTTAGTCTTATTCATAAATTAATAAATAAATAAATAA  
TTGGTATTCATGACAAGACAATTAGTAGAATTTTGTGCTTCTTGTCTGCAATTACAGAA  
TCAATATATTTTTCTATATTATTGTATATTCTCTAAATCTTATTTTGTATAATAGCTTTCA  
GCATGTTCTTTAATTCTGTTTAGATATTTAGAAAGTATTTGTTGTTATTCTGTAATTTAT  
TTCAATATTCAATTATAGTTTAAATATTTTGTATCTAGTGTGTCTTGATTTTGTATATAC  
GTACTGATTTTGTAGATCCAAATTCCTCTTCTCTATCAGAGAATGCAATTTTTTACTTGG  
ATAAATAAGAATCATATCTCTCTGCTTGCTACCGTATTGCATACATTCTGGGTAGAGA  
AAGAGTTAAGCTGATGAGAGTAGGAATTAAGGTAGACCTGTTTGGTAGGTTCTCCAGAT  
TTCAGAGGACAGACATCTTTTTTCCCTGCCCTGGTCAATTTAACTTTTTGGATTTTGGGA  
TTAAGTGTAGGCAGGGAAAATGTATCAGATATTTTTATTTTTCTTGGTGCCATTTGTCC  
TTCTCTGCTTTAGGCAGAGAAGCATATGTAGTCCAAGAATGTGCTTTTCTATCCAGCTAC  
ATCAATAATAACAATTAGTAAATTTCTACTTAACTTAGACCTTTGCTGTTCTCTTTTCT  
CTGCTTGTGTTAAGTCATGCTCATGATTCTGGCAGTTTCCACAGTACCATGTACAGAAA  
GCTTGAATAAGGTACATCTAGAATACTCATATATGTTCACTTCAAAAACACATTTTTGTG  
GAATTTCTAAATGCAAATCTCAATAGTGAATTTCTAATTTACAATGAGAAAAAATAAGGG  
ATTTTTTCTGGTGATTCTTTTTGCTCATTATATAAATATGTTTTTAAATGGTAAGCAAATA  
TATAAATTAAGCTTTTCCCTTACGTAGCTACATTGATTTACTAGTGGTGGAAAAGGTTAAG  
CAAACTAATTTTCTAGTGTAAATGAATTAGTAAGTGACATATGCAATGCTTAAGGGG  
AATTTGCATAAATCTATGACTGATACTCAACCTCTTGCTTAGCGAGAAGATAATTAAT  
ATTTTATACTTCAAGAAGACCTAGTTTTCCAAATATTTACATCCACAACTCAGATTTT  
ATAGCAAGTAAGAAAAGTTAAGTCAGAAGCATATACTATTAACAGCTACTTACATTGCTC  
AAATTTAATATACGATTGCTGCTTTTGTGGTTTTGAAATGTTTCTTGACCATGGATCTG  
AATAATGAAGTTATTCAAGAAGCAACTTTAAGAATGTTATATTTCTTAGAAAAGAAGCTATA  
GATACAATAATATTAATAAATTAATGTAAGTTCTGCACTCACAGTAGAGGTAAGTTCA  
AGGTTATAAGAGAGCTTATAGATTCTGAGATTGGAAGAAGAGAATAGAAAAAATTTT  
CAGATTAAATAATGTGTTAATTGTGCTTCTAAAACAGCTTTGGTGATCTTAATAAATAA  
ATATTGTTTTTATTTCCATTTTTGCTTTTCCAGACAAGAAATGCTACTTGATGGCTGCATA  
TATTTGTTTTGTCTCTTTTACCACCTACTCTTGCTAAATACTCTCAACCCACTCATGAA  
ATTAAAGCACATTGGAAAACATTTATCAACTACCTGTAAATACAACCTATGCTCTCTTTT  
GTGGAGGTGATAGACATTCAATGGAATAGTTGATCTAAATCCTAGTCTTCATTATCT  
TGTTTTATACATTCTTGTCTTAATCAGTTTGGGCTGCTCTAACACAATACCATAGACTAG  
GTGGCTGATGAACAACAGAAATTTGTTTCCGACTGTTTTGGAGACTGGGAAGTCCAAGAT  
CGAATTTTATGTCTGGTGAGGGCTGTTTCCCTAATTAATAAACATCTGTTGTCTCATATG  
TCCTCACATGATAGAAGGGGCAAAGGAGCTCTCTGATGTCTCTTTTTTAGAATATTAATC  
TCGTTTCATGAAGGCTCTGCTCTCATGACCTATTCCTTCCCAAAGGGCCCACTTCCAAAGA  
CCATCATATTAGGGATTAGGTTTCAACAAATGAAGCCAGGGGGAGGTTGGTAAACATTCA  
ATCTATAGCAATGCCTATCTCCAGGAGCTGCCTGTGGAACACTTTTATCTGATATGGTA  
GTTTAAAGCATGGCAGGGATAAGTGGTATGAGGAAAACCTCTCCCTGCCACCCAACGCACA  
CATCCCACTTAAGCTTCAGCAGCTCCAATTTTATCTGTGTAATATTTGGTTCCACATCAA  
AGTTGTTTTGAATATACTTCCATTACCTTAAAAAATGTAAAAACACTGCTTTAAAAAGCC  
AAGCCTATTCCCTTTTCAATTATTCAGAGTTCTTCCAGTTTTACCGTTACATCAAATTAGA  
ACTACATAATTAGGAACCCCTCTCTAAATTTGCCTCTATACAGAGAAAACCTGTGCCTGA  
AACTTTATTAATAAATAAAGGAAATATGTATGAATGTATATATATAATTTCTCTGAA  
GGACAGAATTTGTACTTCTGTTCCATACATAAAAACCTCATTTGACAAATAACAAGCATAGC  
TCCAAGCTCAAAGAATAGCTTAATTTTTCTGATTAGTTTATATCTCTCTTATTAATCAA  
TGACATTTAATATTACAACCATAGCTTGGGGTTTTAGTTTATTTGCTTTCTATCTTTTTT  
ATCTGTGCGCCTACCTGTGCCCCAATATGTTATAGTCAGGGGTTGGTAAAATAAAGACA  
AAACAAATCCTGTCTTCTGGAGATCACCTTCACTGGGGGTTGAGAAACAATAAGAACAA  
GTAGTAAGTAAATATGTACATTAAATTTTTAGATGAAGTTAAGTGCTATGGAAAAAAGT  
AAAATGGAAGAGGTGTTATGGAGTACCTGTTCCGGGTATGGGTTCAATTTACAAGTGGATG  
GTCACCTTCTCACTGATAAGGTGACATTTGAGCAAAAGTCTTCAGCAGGAAGGGAGAATG  
CCATGCAGTTATCTTAGGAAAGAACATTTCCAATATAAGTAACAGCCAGTGCAAAAGCCC

FIG. 1P

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TGATGTAGATGCATACCTTAGGTATACGAGTAACAGTAAGAAATTAGTGGCACGAAAGAC  
AGATGTACTTGGAAACCAAAAAGAATCTCTGGTAAGAAATTGTAAGTCATTGTAAGGACT  
TAAGGTTTTTTTTTTTCTCTCCAAATGAGATGGAGATCCATTAGAAGGGTTTGCGTAGA  
GAAATAATATGATCTGACTTATATTTAACAGGACTACTCTTTTGCTGAATTGAAAATTGT  
CTCTAAGGGTGTATATCAGATCTTATATTGATCTTACCCTTCTCTGTTCAATATTTAACA  
CACAAGCCTGTTAAATAGTCCATTCCCAACTTCTGTGACTTCTTGCTTGAGAGCCTTTCT  
ATCCCCCTCTCATAAGGGCTGTGAGGGCCTAATCTGCTTACCTATCCAGCAGGCTGGGAAT  
GACACAGAGCACTCACCAGGAGCACTCTCAACCTATGACTCATGGAAGTTGGTAGATGAA  
TACCCAGCTCTCATATTCCTTGGGTGGAAGAGCTCTGAGATGTGTGTTCTACACCATTA  
CCCAGAGGGCACCTCTGGATTAGGCTCAAGTTGCTGACAGTAGTATCTTGCTGACTAAC  
ATAATTTTTATTAATTTTCTCCCCATTTGACCTTATTTCTCCATTTTTCTAATAGTGTTT  
ATTGGTATCACTTCCAAAATAAATTACCTTTACTTGAATATTTTTCTTAGAATCTTCTAT  
ACAAAGCCTGAGCTAATACTGGGGCAAAGAGTGGAAGCAGGGAAATATTTTGTAGGTTG  
TGGTGATGTAGGACAGAGCCTGATAGCTTGGATCAAGGTGGTAGCAAAGGAGATTGTAGA  
AGCTATCACACTCTTTATATATTTTGAAGACACAGCCAAGAGGTTTGGTGGAAAAATGGA  
TTGTGAGAAGTAATAAAAAGAGTGGGAGAGAAAGTCAAGGATGTCACCAAAGTTGTCTTA  
AGCAAGTGGAACCTTAGATTTGGGAGAATCAAAAATCCTAAAATATCCAAATCCTCTCCC  
CTGCCCTTCCCCTCCCCTCCCCTCCCCTTGGAGATAGGGTCTTGCTCTGTTTCAC  
AGGCTGTAGTCTAGTTTTGCGCATCTCGACTCACTGCAGCTTCGACCCCTGGGCTGAAGT  
AATCTTCTACTTTAGCCTCCCAGGCAGCTGGGACTACAGGATTGCACTAATGTGCCAG  
CTGATTTTTTTTAGTTTTTTTTTATTTTTAGTGGAGATGAGGTCTCGCTATGTTGCCTGAG  
CTCAAGCAATCCACCTCCTCAGACTCCCAAAGTTCTGGGATTACAGGTGTGAAACACTG  
TGCTTGCCCCAACATTTTTATTTTCAAATATTTAAGTTTTGAATGTCTATTCGATAACCAA  
GTAAAGAAGTCAACTAGAATATATGAGAATGGAGTTTTCTAGAGAAGTCTGGGTGAGGA  
TGTACTTTTGGGAAATGGAGCACATACCTGGTATCTAAAGCTGTGAGCCGAGATGAGATC  
ACTAGGTAGGTAAATATAGATAAATTAGAGAAAATATCTAATAATTGAGACATGGAGTAC  
TATCATAAATTTGAAAAGACAAGAAAATGTGAGAGATCGAGAAGAATGGCTGGGGAAGA  
AGGAATCTAAGGTAGTGAAGAGATTGAAATGTGTCAAGGAGAGAAGAGAGTAATTAGCTC  
AAATGCTACTGATAAGTAAAGTGAATGTAGAATGAAAGTCAACCATAAAATTTGGCATT  
ATGGGGATCATTAATGACCTTAAAGAAAGTGCTTTTTAGTGTAGTAATAGAAAGATGCAGA  
AAGTAAGTAGAGTGAATTCAAATTCACAGAGAATAGACAGAGAGGAATTGAAGACATTT  
ATACTGACAATTCCTTCCAAGACTTCTGCTATTAATAAAAAAATAAAAAAGAAGGAGAAAT  
GGCAAGTGTTTGGAGGCCAATTTATACTCAAGAATAATTTCTTGAGTTGGTTTTTTGTGT  
TTGTTTGTTTTTGATTGGTTAGTGTGTTTTATTTTTTAGACGGGATTGGAGAAATACTTTC  
ATTTGTGTTTTTACCCATGTTTTTACGCTTGGCTGGCTGGCTGGTATAACGCAACTCTA  
TTTTGTATTCTGCTATTATAGTTTCCCTAGCTTGAATTTTTTTACACCCTTATTATAATT  
GTAGCGTTGCATGCCTATTTCAAAACATCTCATGTACCCCATAAATATATACATCTACTA  
TGTACCCACAAAAATTAGAAATAAAAAAATTTAAAAATTATGATTTTTTTAAATTTGTTA  
AATAATGTTTACTGACTCTTTTATTTGTTGAAATCATTCATTTTTTTGGAATATCAGGTCC  
AATTAATATTTAATCAGACTTTGAGAAGGATTTAATAAGACCAATAAATAACCAAGTAT  
TAGTTGAAGGAAATTTAGATATTTTGGTAGCAGAAGGAAGTGAAGTATGGCTCAAGAGT  
TTTTTAATAAGTGTGAGTGGAGTTATACAAACTACTCATTAAATCTTTATTTGAATTTG  
TAATATCTGAAACCATTTTCATATGAAGAATCACTTAAAAATAGTCATAAAATGTAAAT  
TGCAAGACAATTAAAAACAAAAATATGATTTACGACTGTGATAGTACCTGAGAAATTTT  
TTCATCTCCTTAGTAAGAGAAGTATTACACCTATTTATAGTTATTTTATGAAACTAGCTA  
AGATGAATTATGTAGAAAAGATACAGATTTTCAAACAGAACTAGAAATTAATGGAAGCTA  
TGTGAGACTATAAAGAGTTTAATAGTTATTTTGATTTTTTTTTTATGAGTGCAAGGAGTAT  
AGCGAAAAATAGCATCTACCTATAAGGATTTGCAAAGCCAGTAATCTTTCTAAAAATATC  
AGCAAACCCAGAATTAAGGCTTATGTTCTTAGCTCATTGTAAGTATGATCAAAAAATAAGA  
AGGCCAAATAAAGGTATGTGACATTTGTTGAAAACCTGAAGTGTCTATATGCAGAAATA  
TTTTTATCATTTAATTAATTTTCAAGAACTTCTTAACATGACATGATCCTCTTGAAAAGAT  
CACATCAAAAAAGGCAAAATAATTGCATAATTATTGTAGAATAATTTTTGTGTGAGTATT  
TTTGACTTAGTGTAAAGTTTCCAAGTTTCAAGATTTATCATGCAGTGAAAAAAAATACACTT  
GTCTAGAAGACAGGAGACTTTCATTATATTCCTCTCTTTACAATTAATTAACGTAAGACCA  
TTTAAATATGCCTAATTTTCCAGGCATTGGTTTGCTTTGCTATAAAATGGGAGGATAGA  
AAATAACTTTCAAATATCTTATAAATCTAAGAATCTTTGCATCTTATAAATCTAAGAAT  
CTTTGGAAATTCATAGATTATTGAGATGGAGTCTCGTTGCTATGCATTGTAGCAAAGTTG

FIG. 1Q



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GAAATAAATTCTAAATTTTATTTTCAATTTATATTGATCAATAAATTGTTACATTTCACTAA  
TACAATAAGGAAAATTTATTTTACCTGAGTGTATGTCTAGCTTGTGAAATAAAAATGCTC  
AATTATGAAAGCATTATTTGCCATTTTGAATGAAAAATGTAATATGTAGAACAGAATTTT  
TTTGGCCTTGAACCTCAGTTAAATGTAGAAATTGATAAGGACTTGCATTTTCATGAACCTTA  
ATAATTATCTGTCTTTTCAATGGTCTCCATATCAAGTCTGAGAAATATGGATGTGATTTA  
TTTTAAACCTCACCATTTGAAGTAAATCTAAAGATTCCATTAGGTTATGAGCATATAGGA  
TACAAGGACCATATTGACAGTTTTGTGGGATTGTATTAGGATAAAAAGGGTAGGAACAATG  
GGGAGAAAATTATAGCTTACAATAGGGAAGAACCAAAAATTTGTTGCAAAATGATGGAACA  
GGCTGAAAGAATGATATAACCTCCTAAACACTTCAAATGTTTAAGCAGTTCATTGTACCA  
GGGCCATTGTAGCAAATATTTTCTGTCTTGGGTGGAAGGTCAGTCAAGGTGACTGATAAA  
GTTTCTTCTAACGATAAAAATAGCACAACTCACTTTTTTCTAACCTCTAAGAGTATATTA  
ATATCAAAGAAGGCAAGCAACAACTACTTCTGAATGTTAATATATATCTGCATTTCATT  
TAAAAGTCTGCTACAACCTACAGATAGAGGAACAGTTTGTAGTATCCGTGATCCTAGAAC  
AAATTAGCTTTTAAATATCTTGTCAACTTTTTTGTTTTAGTATCTCTTCTTGGAACTAG  
CTGAGCTTTAATGGCATCATCATGTGATGACTTGAGATTATATTTTGAAGAGCTTTG  
AAAAATCACGGATTGTTACCCTAATGAGGTGTTATTCAGTCTTTTAAACAAGAGCAATTT  
CTTTACAAAAGGAGCAGAATTCTTAATTGTATCTGTAAACCTCCATTTAAGAATGAATT  
ACTTGGCTGGGCATGGTGGCTCACACCTGTAATCCCAGCACTTCGGGAGGCAGAGGCTGG  
TGGATCACTTGAGGTGAGGAGTTTCAGACCAGCCTGGCCCCAACACGGTGAAAAACAGTCT  
CTACGAAAAATAAAAAAAAAAAAAAAAAAAAAAAAAATAGCCAGGTGTGGTGGTGTGTGCCT  
GTAATGCCAGCTACTCGGGAGGCTGAGGTGAGAGAATCACTTGAACCTGGGAGGTGGAGG  
TTGCAGTGAGCCAAGATTACACCATTGCACTCCAGTCTGGGTGACAGAGCGAGACTCCAC  
CTCAAAAATAAAAAATAAAAAAAAAAAGAATGAATTGCTCATAAATGTGCCTCACTGAT  
GATTAATTTAATCCTGCAAGATTATGTCTTTTGATGGAAATGAGAGGGTTTATACAAAG  
TTTTATTCGTGATGTTATCTATGTCATCTATTGATTTCTGCTCTGATTTCATGTGGATGAA  
GTTACACCTCACACTTTAAGCTGGTGTGAGTCTTCCATTTTCTGCTGTGATGTGTACTC  
AAGATCTCCAGATTACATCTGTAATGTAATGCAGCCATGATTGTTTATAGGTACATTTAG  
ATGAATTCAATGATGAGTTATGTTGTAATAAGTGTGAGATTTAGATGAACCATACAAATA  
AAAGAACCATGCATTAAAATGACAAATGTGTAAGCATTATTTGGGCCTTAAGTCAAGG  
CCCAATGTGGATACTGGTACTGAGACATCTTTCAGAAAGGAGGTATGAAGTACTGAAAA  
ATATTTACAAAATGAAGACTACTTTTATCTTACTTATCATGATTCTTTTATTACATATGC  
ATTTTCTAAGATAACTATAGTGCATTAGTTTGTACTATGTTAATAATAAATAGGGTAA  
TCAAACATGTTTTCTAAATCCATTAATAAGTATGAGTTCCCTAAGGGAGTTAAACAATTAC  
GTTCTACTGTATATTATTGGCATGCTTCAGGAGACATGATTTAATCTCTAGACTATCAGA  
ATTCAAGAACTAGTGAGTCATATAACAAAGGAGGCTTAATCATGCCATTTAAGTGTGATG  
GAAAAAGGTTTATTGGTCAAGGAAAAATTAATTAGAAAAAGTTATAAAATACTTCACTAA  
GAAAAATAAATGTGAGGAAGCCCACTTAGACAATGAGTGAAAAATGAAACAAATTCAGTT  
TTTACAATATTTGGTTTCTATAGGATTGCTTTCATTGTTTGGTTTTGTTTTTCCCAT  
AGCTGATCTCAGAACTTTTCTCTACATGAAGAGGCTGTGATTTTTTTCATGGTGTGTGT  
TTGTTACATGCCACACAGACAATCAATTATGAAGAAAGGAGAGACTCGTAGGAGGCAGG  
GCCAGGCTGTTTCACTTTTAACTAGGTAGCCACAAATGAGGCTTAGTTACAAAACTT  
GAAACTGGATTCTTCCCAATGTATTATACATCCCCAAAGAAATGATGAAGTTCTTACT  
CTCTTCTCTTTGTTTTTGTAAATCTTACCCTCAAGTGTGGCAATACTTACTTTAAAG  
TAGGTTTTTCATATTGGCTTAGATTTTTTTTTTTCATTAACTTGCAATTTGTGGTTGGGAAAT  
GATCTGCTTTTTTGTTCAGGTTGTTTAAATGTTTTTCCAAATGTAATATTCTTCTGCACTCC  
AGTGAGTTTATTTACAAAACATTTAATGTGATTTGCGTCTTCGAAGAACAAATGTATTCCG  
TTAGAACAAAAGTGAGCTCCTGCATAGAGCTTATGATGGTTTATAATTGGTAAATTATTA  
CCTTGGTCAAGTTTGTAACTAATAAAGGGAGTAGAAAACTTTTAGATAAAAAAACTAC  
CTCATTCAAAGGGACCGTTTACCCACAAAATGCCTTTTTGTTTTATCTTTTGGAAATGACAC  
ATTGGAAACTCAGTATGGCCACTTTTATGGTAATAATAAAGTCATATATAAAAAGGAT  
TATTAGAAATGTGTTATTTCTTAGGCAGGTATGCTTATTTAAAGTATGTATGCATACATA  
CTTTAACTACTAAATACAAATAAATTAGTAGTACAGTCATTAGGATTGCTCTTAGTTTG  
TTAGTGTGGAAATAGACTTTTGGATTTTCTTCTAGCTTAGATTGATACAATGTGATGGG  
GACTTGCTCTCCAAACACAGGAATAGGTGGCCTGCAGACACACTCTGTGATGCTGTAATT  
CTAATCCTCACTGAATATATCAGGGGTGGACATCTGGCCTGGGGCAATTCAGATACTTTT  
CTTAAAATTTATACATAAAATTCAAAAGTGGTAACTCATCTCTGCCATCACTTATAGTA  
GAATAAGACCCACTGTTGCAGTGGGGAATTGAGAAACCCAGTCCACAGGGAGAACAAACA

FIG. 1R



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TGGAGAATAAAATAAGTAAATTAGAACAGGAAAAATGCCAAAACACACAGACATGACCCCT  
GATAGTTTTCCATTTCCCTGATCACTGTCCCTTCCCTGTGGCTGGATAAGGAACGTCTCTA  
GGCTCTGTAAGACATATTTGCATCCTTACGACAAATTTCTACTCCTTTTCATAAACTAGA  
CTTGGGTTCTTTAACTTGCACAGCAACAATAAACGATTTTGTGGGTACAATCTGA  
TTTTATTAACTTCTGGATTTAAAAGCCCTTCTAAATGTTGATTGGCATTGTTTTACTTC  
CTAAGAGTACGCTCATGCACCACATAGTGATGTTTTGGTCAACGACAGACTGCATTTACG  
ACTGTGGTCCCATAAGATTATAATACCATGCTTTTCTGTACTTTTCTATGTTTAGATATG  
TTCAGATACACAAATGCTTATCATTGTGTTATAATTGCCTACAGTGTTTACGTACAGTTAC  
ATGCTGTACAGGTTTATAGCCTAGGAGCAATTGGCTATACCCTATAGCCTAGGTGTGTAG  
TAGGCTATACCATTAGATTTGTGTAAGCATACCCTATGATGTTTGACAATGATGAAATC  
ACCTAAGGATGCATTTCTCAGCATATATCCCAGTCATTAAGCAAAGACTGACTCTATTAT  
TAGGTCTATTTTATTCTATAGCATTGTGATCATGAGATATGTGAAAATAAATATAATTTTT  
AGAAGTACAATAAATCTTCAAATCCTGAATGTTTCTGTACTTTCCATCTCACAAGCATTTTG  
CAAAGCATCAAATGGTATAAGCCAGATTACTGTTAAGGCAACTTGGAAATTAATATGCTGC  
TCAGTTCTGGAAAAGGCATATTCTGTAAATATAGATGAGAGAATATAGACTTTTTCCCTC  
TCTTCTTACAATCCACATTTCTATTTCAGTATTTTCAATTTACTTGAGGGGTTATATGCTACTT  
ATCTTTATCTGTTGTGGAGTGAGGACACATTTCCAAATGCCTTGGTATTATTAAGGCCCT  
TCATGATGTGGCCCCATCTTTTATGACTTTTCCCTTTTCAACTGTGCCCTCTAGCCTTATT  
TGATTTCTCTCAAATTTCTTAAACACAGCATGCTTCACTGACCTTTAAGCCTTTGCACATA  
CAGTGTTGATGTGGAGCTTCTGACCAACTCCTAATTTCTCCTTCAGGCCTCAATTTAAAC  
ATCACTTCCCTCTGGGAAGCTTTCTATTATTTCCCAAGGTACTGGGATATGTTCTTGACAG  
CATGCTGGGCTAATGTCACAATGGCTACCTTGTTTTATTGTTAGTATTTGATCAGCGACA  
CCTTGCCAGGGAGCCCCGTGAGTATTGTCTGAGCAGAACTATGGCTATCTTGTCCCTGT  
TTAGCACAGGGCTTCTCTAAAAGTGGGCTTCTCTAAAAGTAAGTGCTCAAGAACAACAAC  
AAAAGTGTTACATTAATAAACACACACACATACATACAAAGAAATACCTGTCTTTCTCC  
ATATCTCAAGATCATGCTGAAAAGCCAGCATTCTGAACAAATTCCTGTGCGAAGATTGA  
GAATGAAAGATGAATAAGAGGTATCTTTAGAACCAATTATGGCTGCCGTGTTCCCTGA  
GTGTGAGGCTTGCTGTTAGAGTGACAGAAGGAATTTTGACTACTCAAGACCATACAAATT  
TGGAAATGACTCCAAAGTAAACATGGTTAGATAACTACACATTTCCATTTCCCCCTTTTTTA  
TTCTATAGAAATCCCACTTTGTTCAAGTAGTAACATGCCAGCTTCAGAAATGAGTCAT  
GATTTTTCTAAAGCAACAATATCAATCTTCTTTCCCTTCCCCAGTGATTGGTATGGAAGT  
GGACATTTTCAAGCAAGTTTATAGCAATAACGTGAATTCTGTTTTGAAGCATCTAAGAAAGA  
TTTTGCTTTCTGCTGTAAATCAAAGCAGAAACAGGAGAAGATTCTTTTGGGCCCTCTTTC  
CCTCTTCTGGCGTGGAAGTAGTTGTGAGAGCATATGATACCCAAAGTTTCGGTAGACAT  
TTTATAATTATGTGATGAATAACCTAAGGATAATTAACATATAAAAGAAATGGAGAAAGA  
CTGAGTCTGTTTTACTCCACAAGATGCTGAACCAACCTGAGACATAATTTATCTGGATT  
CTTAAATAACTAGTGTCTTTGTGGTTTTAAGCTGTTCTTTGTAAACAAACATATCATAAGT  
GATTAAGTGATGTTATCTTCTTTAAGGCAATCAAAATGCATCTGACAAATGGCCATCTA  
ATTTAAATTTCCAATATGTAGACATCTCAAACAAAGTCAGTATCTCAAAAAATATACTA  
CAAAAAATCTCATGTGTCCATTGGGGATAACTTCCAATGCTCTTTCATTGGTATTGTAGC  
TATGGCATTTGATTTCCAATTGTATGTGGATCAGGTAGTTGCAGGGTGACTCTCAAGGGC  
GAGAAGAAAGTAAGAGTACATGAAAAAAGAGGAAGAGAGAGAGCAGACAAGAAGGAAG  
AACAAGACAAAGTCAAACCTAGGTAGAAATAAGAAGGAGCTAGTACAGAAAGCAAATGC  
CTAAGGTGTTGGAGAACATAGAAAGGTAGAGTGGAATGAAAAAGAAAAAAACACTAAATA  
GCAGCACATAGAATCTTGGGGTTTTAGGGATATTGTTTATGAAAGGTTAGAATAGGCAAC  
AATCTACCTTGTGGCATCTTCTTAAATTTATCAACATATAAAACAAACAATAATTATTTA  
AATTACCTGTGTTATGGGTCTTGTCTATTTATTTATAATTTAAGGAGAATTAAGGAGTAACT  
TAGTTGCTGGGGAGTGACATCAGCAAGATGGAGATATAGAAATCTTCAGGACCTCCTTCC  
GTCCATGGAACCACTGACTCAAAAATGACAAATGGAAAAAATTTACTTTCTGAGAAATCA  
AGAAGCCAGTTAAGAGGCTCCTGTATCTCAGATGAGTGCAAGCCAGCTGCAACAGAGCC  
AGCAGAAAATTTGTTGTACTCACTCTTCATGGTCACTTCTGGCATAGCACAGTGCAATCT  
AGAAGAAATTTCTCGGCTCCTGACTACTTTCTTGGAAAAGAAAGAGAAAAATGTACCATAT  
GTCTAATATTCTGATGGGGATGGGGTGTGGGCTGCTCAAAGGACTAGCTTCCGTCATGCC  
TAAATACAAGTGCTAATTGGGAAGTCCACAATGTTGGGGGCTGCAGAAAACAAGGGCAAC  
AGTTTGGACTAGCATGCACTCATTTGCCGCAGTTCCTCCTCTCACTTCATAGAATGAGTA  
GAAGAACCCTTAATCTCAAGGTTTTTTTCTGGGGAGAGAAAGAGTCAAAGCAATTATA  
CAATATTATGGCTTTGTGGGAGTGATGTATCCAAAAAATAAATGAGTTTTTACCAC

FIG. 1S

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ACCAATCTCAGAGTGCAGATGGAACCTAGCATATTCTAGATGCCTGGGGGCCATTGAGAA  
CAAAAGAGAGCTAGGCAACTTTTACGAGCTCCAGAAGAACTGTGGTACCACAGATAGACA  
CCAAAGGGAGGAAGAGATTACAAGCTCCTGAAAAAAGAAATGAGCAATTCATTCTAATTG  
AGAATTTACACACACTGGTACAGATAAGATGAATTTGCAAAAAAGAATAGAGGCCCCAG  
AATTTCTAGCTGGGTTTTTTGGTGAAGGCCCTTTCTCTGTATCAAGCTAGTCCCTAAAGAC  
TGGGTGAGGTGGTTTTTTGTTTGTGTTTACATTTTTATTTTAAAAGATGGGGATCTCACTTT  
GTCACCCAGACTTGAGTGCAGTGATGCAATCATAACTCACTGCAGCCTCAAACCTCCAAGG  
GTCAAGTGTATCTTTCCACCTCAGCCTCCTGAGTAGCTGAGACTAGAGACACATGCCACTG  
TGCTTGATTAATTTTTATTTTTTTATTTTTTTTTCGTAGAGATGTGGTCTCACTTTGTTGT  
TCAGGCTGGACTTGAATATTGACTTCAAGGGATCCTCCTGACTCAGCCTCCCAAATCAT  
TGGGATTACAGGCATGAGCCACCATGCCTGACCTGTTTTGTTTTGTTTTAAAAAAGTCAAG  
AAAAATTTCAAATAGCAATTATAAAGACAATGAGCTTAGAAAACCAATTAATGGACAAA  
ATGTAACATAAGTAAAGAGATACATGTAAAAAGAATCAAACAAAATTTGCAGTGAAGA  
ATATGATAACCAAATGAATATTACATTAGAGGAGTTTAATACTAGATTGTAACAAGCAG  
AAGAAAGAAATCAGGGAACCTGAAGATGGGTCAATTTGTAATTATTCAGTCAGAGAAACAAA  
AAGAAGACTAAAAAGAGTGAAGAAACCTAAGGACATCATCAAGTAGACCAATATGTGT  
TATCAGAGTTTTAGAAGAAAAAGACAGAAAAATAGGCATAAAGCATCATTGACAAAATAA  
TGACCCAAAACCTCCCAATTATGAAAGACAATAGATATTCTGAATCCAGAGCACAATGGC  
CTGCAACTAAGATGAACCCAGAAAAGTCTATACTTCAAGCATTATAATCTAATTATCAA  
AAGCCAAGGACAAAGGAAGGAAATTTTGAAGCAGAAAAAGAAATAGTGACTCATCAGATA  
CAAGGGCTGTCTAGAGAATATCAGCAGATTTCTCAGCAGAAAACCTTGCAAAACAGAAATA  
AGTGGGATTACATATTCAAAGAGCTGAAAAAAGTCTGCCAACAAAAAATCCTTTATCCA  
GAAGAATTTTCTTCAAATGAAGGAGAATAAAGGATATTCCAGATAAACAAAAGCCAAGG  
GAATCCATCACAATTAACCTGCCTTACAAGAAATGCTAAATGAAGTTGTTCAAGTTGAA  
ATAAAAGAACGCTGAACAGCAACACAAAAGCATATAAAAGTATAAAGCTCATTGGTCAAA  
GATAGATATAAAGGAAAAACAACGGGATATTATAATGGTGGTGGGTAACCTTACTCTTCA  
CCTGGTATAGAAGTTAAAAAAAACCACAAGTATTAAAAATACTGTAACATAAAATTATT  
AATGAATACACAATGTAAAAATATGTAATTTGTGATACTGATAACATACCATGTGTGGAG  
GGGAGAAGTCAAAGTGTAGAGTTTTAAATAAGACTGAGGTTAGGTTTTTATCACCTTAAA  
ATAGATTGTTATAATATGTTTGATTTAAGCCCCATGGCAACTACAAAGAAAATACCTACA  
GGTAATAAACAAAAGAAAATGAGAAAGAAATGAAAGTGTGTCTCAGTCCATTTTTATTTT  
GCTATAACTAAACATCTGAGACTAGGTCAATTTATAGAGAAAATAAATTTATTTCTGCAG  
TTCTGGAGGCTGTGAAGTTCAAGACTGAGTTGCTGCCTCTGTTGAGGGGCCTTCTTATTG  
CATCATAACATGGCAGAAGGCATCACATGACAAAAAAGCAACAGCAAGAGCCAACTGGC  
TTTTATCATAGGCCTAGTTTGTGACACCTTACATAGTCCTATGAAAACCCATTAAGCCAT  
TAGCCCATTAATCCATTAATTCATGAATAGATTAATACATCCATGTGGGGAAAGCCCTCA  
TGACTCAAACCTTTCTCAAAAAACCCATCTCTTAATACTGTTACATTAGTATTAAAGTTTT  
AACATGAGTTTCAGAGTCTAGAAATATTACACCATAGCCTTTACCCCATGACCTCCCAT  
AATTTATGTCCTTATCATATGCAAATACCTTCATTCCATTCCCGTAGCCCCGAAGTCTTA  
ACCTGTTCTAGCACCAACTCTAAAATACGAAGTCAAGAGTCTCATCTGAGACTCAAGGCA  
TGATCCATCCTTGGGCAGGTTCCCTTTTCAAGTTGTGAAATCAAACAAAGTCATATAATTCT  
AAAATACAGTGCTGGTACAGGAATAAGACAGACATTCCTTGTGCGAAAGGGAAAATAAAC  
TAGAAGAAGGGGTTAATGGTCCCCAAGCAAGTCTTAAACACAGCAGGGCACATATTAAAT  
TGTAAGCTAAAGAATACTCTTTTTTGGGTCCATGTTAAGCATTTCTCTGCACAATGTGGG  
GAACACATTGAGCCACTCTGCCCCATGGCTTTGCTGTGCTCAGAACACACTTCAGCTTT  
CTCAGATTGGAATTGCTCATTGGTGCCTGCAGCTTCCCAGGTGGGCACTGCACACTGCT  
GGTGTCTCTATAATTCTAGGATCTCAAAGGCAGCTCTGGCTCTCACCCCGTATTTTTACT  
CAACATTGCTGTAGTGGGGCTCTCAGCCATGGCTCTGTCCCTGTGACAAGTCTCTGCCTG  
GGTCCCCATGCTTTTAGATACATCCTCTGAAGTCTAGGTGAAGGCCATAGTGGCCCTACA  
ACTCTTGCAATTCGTATCCCTGCAGAATTAGCACCAGGTGGACACTGCCAAGGCTTATGG  
CTTTTGCTTTCTGGAGCAGTGAGGTAAGCTACACTTGGAGCCTCTTGAGCCAGTTGGAGT  
GGCTGAGGAATGATGCGCTCACATGAAGGGAGCAGAGGAGTCCCTGAGCAGCCCTGGGCAG  
CAAGCTGTGGAGAGTACCCTGGGCCTGTCCCTGAAACTATTCTACCCTCCTTGGCCCCCT  
GGGCTTTTCATGAGAGGGGGCAGTCTTAAAAATATGCAAAATACTTTTCAAACATTCTCC  
TCATTGTCTTAATGAATAACATCTGACTCCCTTCTATCAGTGCTAATCTCTTTAGCAAGC  
AGTTTTGTCTTACATGGCTAAGCAAGCTGCAAACTTTTCAAATCATTTTGTGTGATT  
CCCTTTAATTATACATCTGTCTTTAAGTCATGTTTTGCTCCTGAATTGGCCAAAAGTAA

FIG. 1T

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CCACACAGCCAAAAGTAGCCAAACAGCATCATGAATGCTTTGCTCCTTAAAAATTTCTTC  
TATAAGATATTTTACTTTATTATTGTCAAGTCTGGCCTTCTACACAGCCCTAGAGTATGG  
ACACAGTTCCAGTAAGCTTTTTGCTACTTTATACCAAGTATGACCTTTATTCCAGGTTCT  
GATACCTTGTTCCTCTCTGTCTGAAACCTCATAACGGCCTTCATTGTCTATATGTTT  
ACTAGTATTTTGGCCATAATCACTTAAATAATTTATAAAATGATTTCAGACTTTCCCTAGT  
CTTCTCATCCTCTGATCCTTCACCAGAAGCACCCCTTAACACTCTATTTACAGCAATATAA  
GATTTTTTTTTGCTGCTCCTCCAAACCCTTCCAGCCTTTGTCCATTACCCATTTCCAAAG  
CCACTTGCACATTTTTAGGTTGAGCATCAGCCTCACTTCTTGTACCAAAGCCTGTATTA  
GGGTTCTCCAGAGAGACAAAACCAATGGGATATACAGAAGGGGATTTGTTAGGGAAATTG  
GCTCACACAGTTATGGAGACTGAAAAGACCAAGGTCAAGGGGACGTATCTGGTGAGAACC  
TTCTCATTTGTATCATAACATGGCAGATGGCATCACATGCTAAAAGAGCAAGAACAATAGC  
CAAACCTGGATTTTATAACAGAGCCACTCTTGACGACTATCCTATTCTGTGATAAGCCAT  
TAATCTGTGAATCCATGAGTAAATTAATCTATTTCATGAGGGCTCTGCCTCTATTGTCCCT  
TAAAGGCCCACTTCTTAATACTGTTACATTGGGGATGAAGTTTCAATATGGGTTTCAGA  
GGAGACAAACATTCAAACCATAGTGATGTCACACAAAAAATTAATGAAACACAAAGGA  
GTACAGTAAGAGAGCAAAATACAGATAAAAGTGCTATATGATATATAGAAAACAATAAAAA  
TGGCAATAGTAGGAGTTTATCTGTCAGTAGTTACTTTAGCCATAAATGAACATAACTCAA  
ACAAAAGACAAAGATTAGCTGACTGGATTTAAAAAATACTATATGCTGTCTACAAGAAGT  
ACAAGGAGCCCACTCCAAATTTGTAGACACACATAGGATAAAAAATTAAGGATGGAAGAA  
AGTATTCCATGTGAATGGTAACCAGATGAGAGCAGGGCTCATTATACTTATATCGGACAA  
ATAAATTGTAAGTCAATAATTGTCACAAGGAACAAAGAAGGACAATATGTAATATTAATA  
GAGTCAATTCACCAGAAAAGATATAACAATTTTAAACATATATGATTTCAATCTTAGGGCT  
TTAAAAATATATAACAAATATTAATGGAAGTGAAGGGAGAAAAGACAGCAATACAACAATA  
GTAGGAGATTTTAAATCTCAGCTTTCTTTTCTAGAGACAGAGTCTCACTCTGTCACTCA  
GGCTGGAGGGCAATGGTACAATCTCAGCTCACTGCAATCTCCACTTCCCAGACTCAAGTG  
ATTCTCCCACTTCAGCCTGCTGAGTAGCTGGGACTGCAGACATGCAACACCATACCCAGC  
TAATTTTTTAACTTTTTGTACAGATGAAGTCTCGTATATTGCCAGCTGGTCTTAAACTC  
TTGGGCTCAAGTGATCCTTCACCTGGGCCTCCCAAGTGCTGGGATTATAGGCATGAGCC  
ACCGTGCTCAGGACCCAACTTTCAAAAATTGATAGAACATCCAGACAGAAGATCAATGAG  
AAGCGGATTGAACAACGTAGACCAATAAGCCCTAACAAACATATGCAGAAAATTCATCT  
AACAGCACCAGAATATGCATTCTTCTAATGCACACACACATATTATCCAGAATAGATCAT  
ATGCTGTGTACAAAACATGTTTTAACAAATTTAAAAATACAGAAATCATATCAAATATC  
TTTTCTGAACACAGTGGAATGAAACTATAAATCAATTATAAAAAGGAACTGGCAATTTCA  
CCAATATGTGTACATTAAACAATAAATTTCTGAACAGTCCATGAGTCAAAGAAGAAATTA  
TAAGGGATATTTGAAATGTTTCAAGATAAATGAAAATGTCTCAAGATGAAATAAAAAGAC  
AACATATCCAAATTTATGGAATGCAACAAAAGTGGCAAGAGTTAAGTTTATAGTGGTAAG  
TGACTACATTATAAAAGAAAAAAGATTTTAAAGTAAACAACCTAACTTTACACCTCAGAAG  
TGGAAGAAGGAGAAAAATACTAAGCCTAATGTTAGCAAAGAAAGGAAATAATAAAAATTAG  
AAAAATAAATTAATAGAAAAGTAGAAAATTACTATAATAATTAATGAAACTAACAGCTG  
CTTTTTAAAGATCAATAAAATTTACAAACCTTTGGCTAGAATAACTAAGAAAAAAGAGAG  
AAGACTCATAAATAATATTGTAAATAAAAAAGGAGCTATTGCAATCAAAGAGGCAGGAAC  
AATAAAGATTTTCAGGCTATTCTGTATAATTATACACTAACAAATTGGATAACCTAGAA  
AATGTATAAATTTCTCAGAAATACACAACCTACCAAGACTGAATCAAGAAGAAATACAGA  
ATCTGAACAGATCTGTAAGTAAAGGAGATTAAATCAATGATCAGAACTTCCCAAAAA  
AGAAAATCCCAGGATCAGAAAACCTCACTGGAGAATTCTGCCAACATTTAATAGAAAAAA  
AAATGCCAATTTCTTCAAACCTTTTGCAAAAAATTGAAGAGGACGAAGCATTTCAAACCTC  
ATTTTATGAGTCCAGCATTTTCTGATACCAAAATGAGATAAAGATATTACAACGAACAC  
ACACACTTTCAAACAAGCTACAGGCCACTATCTCTGATGAATGTAATGCAAAAAGTTGTC  
AATAAAAAATAGCAAACCTGAATTCAACAGTGCATTAAAAGGATCACACACTGTGACCAAG  
TTGAATTTATCTCTGGAATGATGAATGGTTTAAACATATGAATATCAATCAATGTGATACA  
CTATATTAACAGAACAAGGGATAAGATCACATGATAATCTCTATAAATGCTGAACAATCA  
TTTGACAAAGTTTAAATACCCTTTTCGTAATAAAAAATACTCAACAACTATGAATAGAAGGC  
ATGTACCTCAACACAATAATAAAGGTCACATATCAAAAGCTAACAGATAACATCATACTC  
AATGGTAAAAACTGAAAGCTTTTCTCCAAAGATCAGGAACCTAGGTAAGAATGTCCATTCT  
TGCCATTTCTCATCAACGTATTACTAGAAGTCTTTGCTAGAACAATTATGCAAGAATAAG  
AAATAAAAAGCACTGAAATCAGCAAGGAAGAGGGAAAATTATCTCTATTCCCAGATATAA  
TAATCTTATATGTAGAAAATTTCTAAAAATCACACAAGGAAACTGTTGCAACTAGTAAGTT

FIG. 1U

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CATCAAAATTGCAGAACATAAAATCGAAATGCAAAAATCAGTTATGTTTCTATACAATAG  
CAGCAAACCTCTCTGAAAAAGACATTACAATCCCACCTACAATATTATCAAAAATGACTAA  
AATGTTTGTAGTAATAAGCTTAACCAAGGAGGCTAACGACTTATACACTGAAAACCATAAAA  
GCATTACCAAAAAATAATTTTAAAAGACACAAATAAATAGAAAGATAATTCTGTTTTTCAT  
GGGTTAGAAAACCTCGATATTGTTAAAATGTGCACACTGCTGAAAGCAATTTATAGATCCT  
ATACAATCTTACCAAAATTATGATGTCATTTTTTTTCAGAAATAGAAAAAAATCTGAGAA  
CCATGGTACTTAGAAAATCTGGAGAAAGAAGAGCAAAGTAGAGGGTCTCATGCTTCCTG  
ACCTCAAAACATATTCCAAAGCCATTGTAATAGAAACAGTTTAGCACTGGCATAAAGACA  
GATATATGAACTTACAAACCAGCATAGCGAGCCAGAAATAAGCCACACATACATTGTA  
AAATAATATACAAAGCACAAAGACTATGGACAGGATAGTCTCTTCAACAATTGTGTTGGG  
AAAAGTAGATAGCCATATTCAAAGGACTGAAATTAGACCCTACTCAAAAAATCAAGTCAA  
AATGAATTAATAAATAAAGATCTGGGCCGGGCGTGTTGGCTCACGCCTGTAATCCCAGCA  
CTTTGGGAGGCCAAGGGGGTCCAGATCACGAGGTGAGGAGATCGAGACCATCCTGGCTAAC  
ACAGTGAAACCCCTCTCTACTAAAAATACAAAAAATTAGCCGGGCGTGTTGGTGGGCGC  
CTGTAGTCCCACTACTCAGGAGGTGAGGCAGGAGAATGGCGTGAACTCAGAGGCAGA  
GCTTGCAGTGAGGTGAGATCACGCCACTGCACTCCAGCCTGGGGGACAGAGCAAGACTCC  
ATCTCAAAAAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAA  
GAGAAAAGTTTTATACCATTGGTTTTTGGCAATAATTTCTTGTATACGACACCAAGAACA  
GGCAGTAAAAGCAACAAAAAATAGATAAGTGGAACTACATAAAATTAATAAATGATGCAC  
AGAAAATAAATAAAGAAAAAAGACAGAGTGTAAAAGCAAAACCATGAAATGGGAGAGAATA  
TTTGCAAACCATATATCTGATAATGGGTTAGTATTCAAAATATATAAGGAACACCTACAA  
CTCAATAGCAAAAAACTAACCAATTAATAAATGGACAATGGACCTGATGGATATCTCTCC  
AAAGAAGATGTAAAACAGCCAACAGATACATGAAGAGTGCTTAACATCATTAGTAATTA  
GGGAAATGCAACCAAAACCATGAGCTATCATCTTACACCTGGTAGGATGACCATTATG  
AAACAAAAGAAAGAGAATTAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAA  
CCTTTGTACAGCCACTGTGAAAAAATGTTTGGAAGTTCCTCAAAAAAATTAATAAATAA  
CTATACGATCCAGTAATCCCCTTTTAGATACTTTTCCAAAATATTTGAAAACAGGAACT  
CAAAGAGATATTTGCACTCTCATGTTTATTGTAGCCTTATTTACAATAGTCAAGAGGTGG  
AAACAAATGAAATATATAATGACAGATGAGTCAATAAAATGTGGCATGTACATATCATGG  
AATATTATTCAGCATTACAAAAGAAGAAAATCTTATAATATGCTGCAACATAGACAAACC  
TTGAGGACCTTATACTAAATAAATAAACCAGTCACAGAATGACAAATACTGCATGAATA  
TACTTCTATGAAGTATCTAAAGTAGTCAGTCATAGAAGCAGGAAGCAGAACGGCAGCTGC  
CAGGTCTGGGAGTAAGAGTAAGAGGAAAGTTGCATTTTCAGTGGGTATAGAGTTTAAAGC  
ATGCAAGATGAAAAAGCTCTAAAGATCTGATGTACAATAATATGCATATAATGAACAATA  
TTGTACTGTTCACTTAAATATGTGTTAGGTCCATGTTATGTGATTTTTTACCACATTTTTT  
TGAAAGCAAGTTGCTAAAGAATTTGCCAAATGGAATTATAGTGACACGAGTTCAAATAAA  
ATTAATAAACGAGAAACAGTAGAGTTTACTTAATTTGTTAATATATCCATATTATCATT  
TACCTGAAGTAATTTTTTAACACTACAAAAGAGAAAGAAATTTCTTTTGTTCATGATCCATT  
TGTTTTAGTTTTGTTTTCCCATTTTTATGTAGCTAGACTGCCAGTTAATCTCCTAAAATTAT  
TGGCACCATATTTCCCATTTTTCTGGCTTTTTTATTAGTAACTGGGATCCTTGCAGCTG  
TATCTATGTGATGCCAAACAATTAGGTTGATCAATTCTGTGACAACAAGCCATCTGGTTA  
CTTTAGTGAATAGGCCCTTACTTACCTTTCATAAGTTGATTCTATTCTCCTTTGTGCCTT  
CTCTTTAAATTACCATTATCCTGTAACCATAAATTAATAACAGCATCGCTTTTAAAC  
ATCCTGAAGTAATTTTTTAACACTACAAAAGAGAAAGAAATTTCTTTTGTTCATGATCCATT  
GACCCTAATTAGCATTTAGGAACAACTACACTTGCAAAATTAATTTTCGATTGGTAGAGG  
GAAGAAAAGGGTCTTTTTATTACTATGTATTTGTAATTACTTTTGTCACTTATGTTATTC  
TTGTGTCTAAATTCAACTCTAGATTTATTCTCTGTTGATATTTTTTATCACTTGAGAATA  
TTTTAGTTTTTCAACCTCTATATGGCGGGCTATCACTCCAAATTTAGGTTAACTGTAGG  
TTGATTTAAAAATCTGGCTATGATGCAGAAAAAATTCGGGCAACTTACCTAGAAAAAATA  
AGTAGTTATATTTTTCAGTACTTCTTTTACCTAATCAGCCATTTTAAATAATTTTGTTCAT  
TATCAATATGGAGGAAATTAATTTATATGCAGGGAAGTTATTTATATGCAGAGCTGTTAAT  
GGCAGCAATCTGCATGACAAATTTCTACTTAATAAGCAATGAAATAGTTGGATAAATGTG  
TATTTCTACATGGGTGAATTTCCCAAAATTCACACTTCAAAGACAGTTGCTGACATTTTT  
TCAATGAGAGATTTTATTAGATAATGAGTCATCTTAGAGTTATCTTGTAGTATTCTTTA  
GTCTTAATTTAAATTTAAATGAAAGTCAATTCAAAGTGTGATTTTCTTAAATAAATTT  
GTTTTTATAACATATAGAAATTAATAGGACTACCATATGGTCTAGCAATCACACTTCTG  
GGTATATATCCAAAGAAAATCAGTTTCAAGTATGTCAAAGAGATGTTTCGTATTCATTGCAG

FIG. 1V

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CTTTATTACACAATAGCCAAGATATAGAATCAATCTAAGTGCCCATCAATGGATAAACGTA  
GAAACATGGGGCTGGGTGCGGTGGCTCACGCCTGTAATCGCAGCACTTTGGGAGGCCGAG  
GCGGGCAGATCACGAGATCAGGAGATCCAGACCATCCTGGCTAACACGGTGAAACCCCAT  
CTCCACTAAAAAAAATACAAAAAAATTAGCCGGGCATGGTGGTGGGCGCCTGTAGTCC  
CAGCTACCCGGGAGGCTGAGGCAGGAGAATGGCGTGAACCCGGGAGGCGGAGCTTGCAGT  
GAGCCGAGGTTGTGCCACTGAACTCCAGCCTGGGCTACAGAACGAGACTCCGTCTCAGTT  
AAAAAAAAGGAAAGAAAACGTGGTATATATACACAATGGAATACTATTTAGCCTT  
TAAAAGAAGGAAACCCTGTCAATTTGCAACAACATGGATGAACCTGAAAAACATGTTAAG  
AGGAACAAGTCAGGCACAAATACTTAATGATCTCGCTTATATGTGAAATCTAAAAAAGTT  
GACTTCATGGAAATATAGAGTAGAATGGTGATTATCGGGTGCTGGGAGTTGGGGTAAGAT  
GTGGTTGGGGAAACGGTCAAAGAATAAAAAATTTCAGTTAAAGAGGAAGAATACATTCAA  
GAGATCTATTGTACATGTTGAATATAGTTAGTAACAATATTTTGTATCCTCAAATTGCTA  
AGAGAGTAGATTTTAAGTGTTTTTGACACAAAAACTGATAATTATGTGAGGTAATACATT  
TTTTAATTAGCTCCCTTTAGCCATTCCACAATGTATACATCTTTTAAAACATCATGTTGT  
ACATGACAAATATATACAATTTTTATTTGTCAACTTAAAAAATATTAAAGATTTAATGTA  
GATAAATGAAAGAAAATTAGGAATTAAGGTACAAAAATTTATTTATAGTGTTTATTATTGG  
TCTATGTTTACATAGTATTTCTTTGTCTCCATTAGTGTTTATACAAATACCCAACCTAGA  
AACATGACTTTACAAATGGTGTATCTGATCTTTTATGTCCCTAGTTATTATTTTAGCCCT  
GTCCTTTTTTTTAAATAAAACATATTCTGCTTTTTCTTGTCCCTCATCCTTCTATGAGTTGA  
ATTAGTGACTCTACTCCAAAGTAATGGTGTGCTTTCTCAGACCATATGGTGATACAAAG  
GCATATGAGTTATCATAAGCATGGTCTGTGTAGGCAAAGCATGTAACCTCCACAAATGCTT  
CTTGAGAGATTCTAATATAATCTGTGCCAGACCTGCACAAGGCATAGAGAATAAAAAATTT  
GCACCCACACAGTCACTCCTCATTCAATTCATTCAACAATAATCAAGTACCTGGTAATGC  
TAATGCAGTGACTATAATTCCATATACATAAACTAATATTTTTAAGATACATGAAGGTT  
ATGTTATAACTAATAGTCAATGTATTTTTAAAAATTAAGTGAATCAAATTGTAATTGTAAT  
TAAGTATTTTCTTAATCAACAGAACTAAAAGTATAATTTCCATCAACTCCTTTTAAGTA  
TAAATGTAATTAATGCCTGGCACATTCTTCACATTATATAAGGATCTTTATACTTAAGA  
CATTTGGGAAACCCTACTTAGGCTTATCATTGACAAAACATTTTCAAATCTTTTCATTT  
GGTCCTCACCACAATACTGTTAAAAAGACAGCCTAAGCTGTTTTGTGCTTCCTCCCTAGT  
TGGGCATCCCTGTGCAATGAGAGGGACAAACAAGGTGGTTTTAAGGTCAGAAACATCCAA  
TTGCAGCATCATTGGGAAATTTGTAAGAGCAGCTTTTATAAAATGTCACCAACTCATGTA  
TCTTTAAAAGATGTGCTGAATCTTATGCCTTGAGATTTTTCTTAGTTTCCTTATTTTCTA  
TTCCCTCCCACTTTCTCTTTGTCCCTTGGTGGCTTCATTAAATCCCATATTACAATACAA  
AGTAAATAATAGTGCTCTGAAGTGCTTCCTATTTGTTTCAGGATGAAGTCTGAAAAATGAA  
ACTGCAATTTTTTTTCTTTTGAGACAAAGTCTCACTCTGTTGCCAGGCTGGAGTGCAAT  
GGTACCATTTTCAGCTCACTGCAACCTCCGACTCCCAAGTTCAAGTGATTCTCCTGCCTCA  
TCCTCCCCAGTACCTGGGATTACAGGCATGCACCACCACGCCCTGGCTAATTTTTGTATTT  
TTAGTAGAGATGGGGTTTACCATGTTGGCCAGGGTGGTCTCGAGCTCCTAACCTCATCA  
GATCTGCACACCTTGGCCTCCCAAGTGCTGGGATTACAGGTGTGAGCCACTGAGCCCTG  
CCAAAACTGCAATTTTATCTTAGGGGACAGGTAAGCATAAAAACATCCAAATCATGTA  
TTTATGTTTAGGCTCTGCTTGTAGAGTGATACCAAATTCAGGTGTTTTTTTTTTTTTTT  
TTTTTTTTTGGAGACAGAGTCTGGCTCTGTGCCCCAGGCCCTGGAGTGCAAGTGGTGAGATCT  
CGGCTCACTGAAAGCTCCGCCTCCCGGGTTCACACCATTCTCCTGCCTCAGCCTCCCGAG  
TAGCTGGGACTACAGGTGCCCGCCACCACGCCCGGCTAATTGTGATTCTTTACATTATCA  
AAGAATTGATGAAAACAGGATATGAAGATTAGTGAAGGATTCTTTTCATTAGCAAAGTAA  
CTTTTCTTATTTCAAATTTAACACATCTATTTATAAAAGTTATAGAATTTAAATTTTAAA  
ATATGAATGAAGAAAAACAAATCAGCATAACATAGTAATACATATAATTGATATGTACT  
ATTCTGTTACTTTGGATTCACTTAACCTTGCAGTATTCTATGATTTTTTTTTTAAATCC  
ATGTGTTACAGTTAGGGCTTAGAAAGATTTAAGCACCTAGCCAAAATTTATGCATTATGTT  
AAGTGGTTGATATCCACTTATTGACAAATATGTATTGATTGAGAATTAGTCATGGAGATA  
TCAATGGGTTATTTTGATTACTTTTTCCATTACTCCCAAGTGGTCAGGATTAGTTTTAGA  
TTATTTAAGTAGGTTGGCTGAGTTCACAAAAGCTATTACTATGGGGACCTTAATTGAAAT  
CTAACTCTATCCAATTCTATTTCTTTTCCCTATCCCTCGAATGGGTGTATGTGTGTGTGT  
GTGTGTTTGCACACATAAAAACTGTTCTAATTTTATGCAACATGGAAAGCATTAATGTT  
TAACATGTATGTTTGAACAGGGAATTTGTACTGCATTAAAGATTATTCCTGTGTATTAC  
ATACAAATATTTGACTATTGACTGTCTTAGTATGTTTCATCTAATTGTTTCCTATTC  
CCATGAAAACGTATCAGTCTGAGAACAGCTACTATATGATATGCATCACTAGTCTCCCC

FIG. 1W

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ATGGTGCATAATACTTGATATAAATTAGATGCTGTTGGTTATACTTGGCGGGGGGAAAGG  
GGACACTAAAAAGGAAGAGTCAATTTCTACTGTGAACAAAGCAAAAGCAAAAGGAGAGA  
TAAATGGAATTAATTAATAATGAAATTGAGAGTGTAGATAAATCTATGTAATGAAGATG  
CTAGTAACATAGGAAGAGAAATAAGATAGGGTATAACAGTGATTATTTTTCTTAATAAGT  
AGTGTCTATGGCAGTTGGAAGACAAGAGATTATCCAAGCACTGGTTATAGTCTGAAAGATG  
AGGTGGTAGCTTACTTGTGGGCCCTCAGGCATTGCAGTACAAACAGACAGTGAGGGAGG  
AGTCAATTAAGACTTATACAAATGCAGAAGTCATGGTTGAGGTAGTGAGAGGATTTCCAG  
GACAGTGATGAATAACAGAACCTCAGCAGAAGGAGCATGTGGACCCAAAGCATCATACGA  
ATAATGATAGGACCAAGGGAAAAGAAGTCAAGCGGAATGGGGATAGACAAAAGTTTTGAA  
ATTTATGTGTAAGAGTTGAATGAAGAAAGTTATTAATAAGACTTACACAACAAAGAATTT  
CTACATAGAAGTTGAAAAGACAGCAACAGAGTTTAGAGTTTAGGAAAAAAATTAATAT  
TAAATTTTAATATTAATATTGTAGGATTTGAATACCTTAAAGCTGAAATTCAGTTTTTG  
ATGCTGCTTCTTAGCATCTTTGTCTTGACATGTATATCAAAATGTAAGAATGTCTGTATC  
TTACAATCTGTGATTCTTGAGAAGTCAATGCCATATTATTCACATACATTCATTCTTTCTT  
ATTGGAACCATAATACTTTCTTCAATAAATATGTCAGTAGACATTCTAAATAAATAAAAA  
ATATCCAATAACATGCCCCAATGTTTCACAGGTATCACACCAATAGCCCCTGAGATATTG  
TCACATATGAGCAATTTATCTGCAGAAGTCTTATCACTTTCTGTATTAAGTACCAAGAAAT  
TCTTAGGCAATTAGTAAGTTCACTTGTATTCTTAAACTTCACAGAATGAAAAATTAATA  
ATTTTAATCTCTTTTCTAGAACAATTGTTTTACAAAGACTTTTCAAGGTTTTTAAATCC  
TATTTTTTGACAAAATAACATATTTTAATGAAAGTAAACATGTAGAAATGACTTAACCAA  
AACTAGCTATTGACAACCTTTTCAGCACTTTTTTTGGGTGAATTCAGGAACAACTTTGT  
ATTCATTTTATTAATCCACTAAGTAGGGTTGCTTCACCTTCCTTGGTTACTGTGCATGTGG  
ACGAGGCTGATTTTCAATGCTGGGATGTTAAAGGAGGGATTTTTGCAAATCAAACACAG  
AACCATCACCTCACACTTGTAGGATAACAAACATTAGCAAAACCAAAGATGACAAATGC  
TAGCAAGGATGTGGAGAAATTGGAACCTCTGTATATGCTGACAGAAATATAAAATGATGC  
AGCCACTATAAAAAATTTTTGTTTTGAGAATGTGTCTTGCTATGTTGTCCAAGCTGGCA  
TCAAACCTCAAGACTCAAGTGATCCTTTACCTCAGCCTCCTGAAGAGCTGGAACATAG  
GCATGAACCACTGTGCTGGCTTGGAAATTTTTATTTTTCTCAAAAAATCAAAAAATAGAA  
TCACCATATGAGCCAGCAATTCCATTTTTGGGTATATATCCAAAATAATTTAAATCAAAA  
TGTTGAAGAGATATCTGCACCTCTCACATTCATTGCAGTAGTCTTCACAAAACAACCTAAA  
TGTCCATCCATGGATTAATGGGTAAAGAAAATATGGTCTACACATACAATGGAATATTAT  
TCAGCCTTAAAAAAGAAGGGTATCTTTCTGAATGCAACATCATAGATGAACCTGCAGGAC  
GTTATGCTAGGTGGAATAAGCCAGGTATAGAAGGACAATTATTGCATGATTCTACTTACA  
TTAGGTATTTGAAATAGTCAAACCTCATGGAAACAGAGACTAGAATGGTAGTTGCCAGGGG  
CTGGGAGGAGGCAGAAATGAGGAACCTGCTGTCGAATGAGTATGTAGTTTGAATTATGAAA  
AAATGAATAGGTTCTAGAGATCTGCTGTACAACATTGTGCCTACAGTTAATGATGCAGTA  
TTATGCACTTAAACATTTATCAAGAGAGGAGATGCCATGTTGAGTGCTCTTTTCACAATG  
AAAGTACAGTAAATGAAATGAAATATACAGCAGGCTTTACACACACCGCTTCACAGGCA  
AAAACCTACTTGGGAAACAAAATGGAAGGTCCCCAGAGTCGTGAGGGAAGTAAGGTATGGT  
ACAGGGTCAAAATGGCTGTACCTGGAGCTCTCTGACTGGTCAGGCACCAACCAGCAATAC  
TCTCATGCCTTAATTATAGTTTACTGCTGAGATAATTGAGAATGAGAGCTCATATTTACT  
AACCAGGATATGAATAGACTGAGAACCTTTAAATAACTTTCCCTTTAATTCCATAAAAAATCT  
CCATTCTGTTTTAAAGTCTTTAGTACAGATTTTAGATGTAATAAACTGCTAAGATTTGAG  
CAACAACATAAGCATAATAAATGGTTTTGCTTTATGGGCAGTTTTACACTAATGCCTCTA  
ATAATAATAACAGTAGCAATAACAAAATGACAGGATTCCTTAGGACTTCATTACTCAGAG  
CATAATCCCTAGAAAAGCAGCAGTCATTATCTAACCAGAACTCCCAAGAGTTTGCTTAA  
CACTTTAAATGTATAATCTAAATTAAGAAAATATGAGTAAATGGTATTGTTTCCCCTG  
AATTGAAGTAATATGGGATGTGTTGAAAGAATACATCAAGACATTTTTCTACTGTCACCTA  
GCCTGATGACTGACATAGATTAATTACTACATAAATTTCCCTCTTCCATTTAATACTGATA  
AACAGATTTATGGGACTTAAACCACAGTACACAGTTTTGTATTTGTACGAAATGGATAA  
TCACATTTTAAACATGTGTAAGGCATATTTGCAAACCTTGAAACGTCGTCTTCCATAAAT  
ATATGCTGAATGAATGAATTAATGAATAAAAATGAGGCAAAACCTCAGGTGTGGCTCAG  
TCATCTGAATGTTATTTATCCAAATGAAACAGGTCAAAGATTTTTTTTTTTTTTACGGTTC  
ATTTCTAGCCAATAAGACCAAGGTTCAATTCACCTCACCTCTGTATAGAATCCTTTGTGG  
GGGCTGCGAGGAGGCAGTAAGAAGTATCACATCTAATCTTTTCCATAATTAGCCAAGTTA  
GTTGGTACTTCCCATAACTCTGATACCCATAGGCCCTTGCTATTTCTAGACTTGAGTGTG  
ATTCAGAAATATGGTTTAGGCGAGCACTAGGAAAGATACACAGTTTTTCTAAAACACATT

FIG. 1X

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ATCCAATCAATATTCTACTTATAAAAAGTCAACTACACACACTTCAGTCATGAGGTAAAAA  
AATGAAATTTATACATAACACTCACTTATGTTTATCACTCACTTATATTTATAATAATAG  
ACATACAGGTATTCTATTAAAGGAACCTTTTAAATGTTTGACCAGAAAAAATTTCAATATC  
CCTTTTTTATTAAGTTTAAAGTTACTGTAATGAAATTAAACATGTGAAGGGAGACTAATACT  
CTCTTTTAAAGAGAAGTAAGAATGAAATATCCATATAAAAATACACTGCATTATTCTCTTTG  
TTTCAATGGCAAATAGAATCAAAAGGAATAACCCACTTTATTTAACGGAATATCTGAAAG  
TGTTCCACTTATTTATTTCTAATTTTAACTATGGAAAGTACTTGCATTTTTTTTTTAGGAA  
AGAAAGCCAAGATTTTATAAAGTAAAAATCTGCTTTGTGTGCCTTTCCAAATTAGAAGAG  
AAATGTATCATCTTAATACAGCAGATTCACTTATTATAAAGACCTACTCCATCCAAAAAA  
TTGAGTGAAATAAAAAGAAATTGACTTACTTGTAAAGAGAAAAAGATTGCCAAGGCTTGC  
AGACTTGTGAGGTGGTTAAATAACAACTAAAGACTAGCGAATATGAGCTATTTTGTGTTG  
ACGTGCCTTCCATTTAATAAATGCTGTATCAATCTAGCTGTTTCTCTATTTTTAATCATA  
CATTTTGTGTTGCTCTAAATTTAATCTTACCTTATACATTGTATAATAGATGTCCCTTA  
AATACATCAAATTTAACGTGTTCCAAAGAAAACTCATAATCTCCTCATCTCCATCCACCT  
CACTCCTCCTGCTGTGATCAGTCTCTCCGTTTGTTCATTGTCCATCATCTTCTACAGA  
ACAGATGTGCTCCTAACCCACTTTCCTAAACACATTTTGTATACAAAATAATTTCTCTTT  
TTTAATTTCAGAACTCTATTCTGACAAACATTTGGCTTCAACCTGTAATTAAAAACTTAA  
CAATACTTAATAGTTGCCTCAAAGAGCATCCCTCTTTGTCAATGTGAGACTATTTACAT  
TAATTTACATGTAATTCAGTTTCATACTCATTCAGTGGGGTGTGAATATTAGTCAAACGG  
GCAATTAATTAATACAATCTTTATATATTCATTATTAAAAATGCACCACACAATTCCTAA  
TTTATTGAGAGTTCTCATAAATCTATGGGATGTAAATTTTGAAACAGCTGCAGCTGTTT  
ATGCCATTGCTCTTGTGTCCAATAGAGCCAAGTGGACATTCTTTTTTGTGTTGTTCTT  
TCCTTGAATAGAGTCGAAATTATGAATCTAACTTTCTCCGACATGTTGTCTAAAAGGATA  
TCATCTTACCTTACTCAGTGTGAGCCCTAAACTAGGAAATGTTTATCAATCTCTGATTG  
CAGATCAAGTTTAACTATCAAATACAGATTAACTTTTCAGCAAAAATTTGTTAAATATTC  
AGAGATAGAAATCTTGATGTTGGATGACAAAGATCACTTGTGAAGAACTTTATTAAGTTT  
TATTGGTTGAAAAATCTATAATTTTGTAGTGAACAACATATCATCCATTATGTTCCAAGCT  
TTGTGACAACGTTTTTTATGTCCATTAAAAACAGTCTTATAAAAATAGGTACAAGTATCTCA  
ATCTTATACATGTCAAACTAAAGCACAGAGATGCTAAATAACTTGACTAAACAAGATAT  
TGAAGGTGAAGTCTGAGATAGATTTTTAACTCCGAAGTGCATAAACTTTACCTCTATATT  
ATCTGTCTTCAAAAAGAATGATTTTTAAAGATTAGGCTTTTTTATTTTCAAGAAAATATT  
TTTACACAATTCTAGATTCTTAACAGTAATTTGAAGGAATGAATGTCTGATGATTCAAGA  
AAAGTGAGGTACATTTTTAAAGGAAAAGTGACAGACAAAAAATGGATTTTTGAAAAATGAA  
TAAAGCTGCTTTTTTTTTTTTTGATGGTGTCTTGCTCTGTTGCTCACGCTGGAGTGCAATG  
GTGCAATCTCAGCTCACTGCAATCTCCGCCTCTCGGATTCTAGTGATTCTCCTGCCTCGG  
CATCCCAGTAGCTGGGATTACAGGCGCCACCACCAGACTCAGCTAATTTTCTGTATTT  
TTTAGTAAACATGGGGTTTTTACCATGTTGGCCAGGCTGGTCTCAAACCTCCTGACCTCAGG  
TGATCCACCCACCTCGGCTTCCCAAAGTGCTGGGATTACCGGCATGAGCCACCACGCATG  
GCCAAAGCTGGTTTTTAAAGGGATCATTTGTACATTATTATCAAATTTTCAATTTGAACGTC  
AAAAATTCTGAGGCAAGAAGGAAATTGAGCCCAGGAGTTTGAGACCAGCCTGGACAAAAT  
GGCAAGACCCCATCTTTACAAAAACAAAAATAAAATAACACTAGCCAGGCATGGTGGTGC  
ACACCTATAGTTGTAGCTACTTGGGAAGCTGAGGTGGAAGGATTACTTGAGTACAGAGAA  
GAGGTTACAATGAGGGAGGATCGTGCCACTGCACCTCTAGCCTGGGCAAAAGAGCAAGACC  
CTGTCTCTAAAGAATAACAAATAAAATAAAAGTCTGGACAAGCCTAAAATCAGTAATA  
TTTGGGGAATATGCAAATAGTCTTTGCTTTTATTACTCAATTATTGAACTATATTCAAA  
AATAGGAAGTAAACATGATTTAATATTATTTAGTAAGTTAAACATGTTATAATAATTTG  
GAAATCCATGTATGTTAGTTAAATATACATTACTATAAAATGTAAATCAGTGTGGTTTGT  
AGCAGAGACCTGGATTTTTTATCTTTGTAGTGTACCTACACCATCACAGAAAGGTTTGGC  
ATCAGTCTCTAGATTAGGTGCAAAATTCATTTAATGTGATCCATCCTATTATCTAAAAGGT  
CATTTCTGTTGTTTTTTCAGCCTTCATCTAAGACACTCTCAGATACTATTTTCAGGAATTTATG  
ACAGCAAAATGATATAAGGTGACAAAGTAGAAATAGGTGCTATGCTGCTTTACCTATATT  
GAGTTATTTTCTCTCTCCAGGATCAGATATTAATGATAAATTTCTTAACATCAAAAAAT  
AAAACCTAGGTCAATATAAATTTTACACAATCAATGTCACTCAGCAACCATTGAGAA  
TCTACTATGTTTAGAATGGAACACCTGACTTATAGAAAAAAGGTAAAAGATTGGTTTTG  
TAAAATGACACATACAATTTAAGAAAAAATAGGCTATCTATATTAGATAGTTAAAAGAAG  
ATTTTAAAATACGATAAGAAGAGAGGGGAGAAATGGCTAGATTAATTTGAGGATTACCTA  
GTGTTAAAATAAGTCCAGATTTAAATCAAGTTTATTAATTCTGAAAAAGATCACATCCTA

FIG. 1Y



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AAGAAGGCATCAAATTGACCCATAAATGTGGATAAAACTTCTGTAAGATAATGAAAGCCC  
TAGAGAGTAATGTTCAACTCCATTTTCTAATTGGCAACAAATGTATAATATGGGTACACC  
AGAATATCTAACTCAAAAAGTGGGGAAAAAACTCAAAAAGTACGAAATGTTGGCAAAAA  
TGCAGACAGCTAGGACACTCATACCAGCTGGTAAGTGTA AAAACTAGTACTGCACCAAGC  
ACTTTAGAAAACCTTAACGGCAGTTATGTAGTAATGGTGATCATATGCATACTCTATGATA  
GCAATTTCACTGTTAGATATATAACTAACAGAAATTTGCACATATGTGTGCAAGACGTA  
CATAAGAATGTTAGTAACAGCCCTGTTTACAATAGCCCTGAATTAGAATGAACCAAAAT  
TCCATCAATTGTAGAGTATTTCAATGATAATATAATCACACACTGGAATGAAAATGATGG  
AACTACTACTAAACATACAACCTGGATCTTACAACATAATCATAAGTGAAAGAAATTAG  
ACACAAAATAACACATAAATGTTGATTCCACATAGATAAAGTTAAAAACAGATAACAATT  
AATCTATGGTGTTACAAATCAGTATACGGATTTCTCTTTTGTGGCAGGGGGGATGTTGTT  
GGAGAGGAAATAGGAAGAGAGCTTCTGGGGTGCCGGTCATATTGTA CTCTCAGTCTGAA  
TAGTAGTTACAAGGGTATGTACACTCTGCTGTAATTTGTCCAGTGATACATGATGGTTTG  
TACATTTTTATACATGTGTGATAATTCAATAAAAATATCTGAAAAGCTACAACAGCAGTG  
GCAACAACAAAGCCCATTAAACCACAAGAAATAATCATGTAAATTGTTTTCTTCAAATAAA  
TGTGTTGTAAATAACTTCTCTCACTCTTTGGCATATATTTTTGTCTCTTTTGATATACC  
CTAATTTTAGGTTTGTTTAATTTTTCAAACATGTCCTTTATGTTTAATACATTTGAGGAA  
ATCTGCTTAAGAAATGCTTATCTACTCCAACATCTTATCAATGGGAATTTTATTTTTTTA  
ACTGTCAAATTTAGATCTATAAGTAACCTGGAATTTATGTTTGTATATGATGTGATGTAG  
AAATCAAATTTTTATTTTTTCTATGTAGATATCAATTTTATTCAGTATCATTTGTAGAAAA  
GATACTTCTTTGATAATGCAGTACATGGCACTTTTGTCTATGTCAAGAGTCCTTATATA  
CGTAGGTGTGGATCTCAACTATTTTTGTTTGTGTTTTGTTTTGTTTTGGATCTCAATTTTT  
ATTCTATTCCCTTGATCTACATTTATATCCTTGTAACAGTACTATACTGTTTTGTTTACT  
GACACTTGTATTAATATTTGATAGCTAATGTAAATCCTTCAAATTTGTTTTTCCATAAT  
ATAATACTGACTAATTTTGGCCCATTTATATTTTTATATAAATTTGAAATCAGCTTGCCA  
GTCTTTACCAAAGGAAAGCTAGCATTTTAAATTTGGAATGCATTGAATCCATATATCAATT  
TTAGAGAAAACCTCACAGCCTTACAATACTTATTCTTCGATTCCATGAGTAGGGTATATCC  
CCCTATCCATTTAGGTTATTTTTCATATTCCTCATATTTTACAGTGCAGAAATCATGTGT  
TTCTCATATTTTTTCCCTAGATGTTGAACATTTATTATTCTATTGTCAATAGTATCATC  
TATTTAAATGCAATTTCTAGTTGTTTTATTTAATAGAAACATAATTGATTTTGCATAT  
ATACATTATATTTTATATATCAATTTTCATGTGCTCTTATGTTACATATTGTTTTATATTC  
AGCAAGTGTTACTAAGGTATTTATTAAGATTAGTAGTTTATCTGGAGATTCTTTACACT  
TAATAAGTATGCCCTCTGTGGATAATGATAGGTTTTATTTAATCCTTTCCAAACTTCATT  
ATTTTATTTATTTTTTATTGCTTTATTACCTTGCTCCAGCACAATGCTAAATAGAAATTA  
CCATAAAAGACTTTGTGCACTTACTCCTGATCACTGAGGGAAAGACTATTTATGTGAATT  
AGTATTTGTAGATATTAACCTTTGAGAATTTAGCTGTCAATCCCAATATGACAACCTTGGA  
GGTGATGCATTTTTTTCTTCTGCTTTAAGATTTTCTCTTTCGTCAGTGGTTTTTTCAGCA  
GTTTTATGATAATATAAGTGGGTGTGATTTTCTCTTATATTTATCCTGGTTGAAATTTAT  
AGCACTTCTTATATCTACAAATATATACCTTTAATTCGTTTTGAAAAATTTCTTAGATAAT  
GTATTTGCCTTGCCAATATCTTTTTTAAAGATTGCTTTTGTCTCATGCTACTTCTATACAC  
ACATATTGAGAATCCAATCACAGGTATAATAGAATTTTCACCATGTGTTATGCACACTCT  
TCTGCATTTTCTTTTTTCTCTCTCTGTTCTTTAGCTTGATATTTTCTATTAGTTTGTAT  
AATCCTATTAGATGGTTTTTATCTAATCTTTCTTTCTGTTAAATCTCTTTGTTGTGTTTCC  
AGTTTCACATATTTTTAAGTTCTATAATTTCTTGGACTATTTTTCTATTTTTTATATTCT  
TTATAATATATCTACTTTCTTGACATTATTAATTCAATCATTTTAAAATTTCTGAAATAT  
TTTATGAAAAATTTAGAAATATTTTTATGTTCTAGATAATATTTATCTTCTTTCACAGAG  
AATTTGCTTTTGTCTTTGGCCAGCAGCTAGTGTTGGGACAGAAAACCACTATCCCGTCAGT  
CACTGGAGGCTTTGGAAGCTGGGCTTCACTCTTTAGGAGAGCTTGCTACTTCAGATTTA  
TCCCTATCAGAGTTCAAACTTGGAGTTACAGCTGAAAGCCAGGGTTGTTTACCTACTTG  
ATAGGCCTTGAACCTCAATTATCATCTTATTTTTGGTTAGGTACTAAATTTCCGGCTCAG  
CATCTCATATTATCAGCTTTGTTCTCTGTTTCTCTTCTCTGTTCTTAGCTAGAGTTTGC  
AAATTGCCAAAAACTTTGAGAAGAAAAGAGGCTAAATGCCAGAGCATCTCCCTCTTGCAT  
TTTCTCCAGGATATTGGCCTTTGATGTCCCTTCTGCCTTAGTAGCTTTCCAATGTCTTAA  
AGAAATGTGTAACACTTCTGGTTGTTTTAGGTGGGAAGTTGTTCTGCAGTAAGCTTATC  
TGCCGTTACCAGAAATAGAACTATTTTTGTAATAGTAAAACAAATGTATACTTTCTGTA  
ACAATATTTAGTACTTCAGAGAACAATTGGCACTTTCTGGATATTCTCAACCAGGAGTAT  
GTGGTTGAAACTGCACAGTTTTCTGGAGATGATTTAGGTTCTTCCCTTCTTACTCTAATT

FIG. 1Z



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CTGTCACTGGTTGATCTTATCCACTCCACAAGCTTTAATCACAATTTCTATTCTGATGAA  
TCCCAAATATTTACATGTAAAGAAATTATATCCCCTGGAGTATAGAACCATAAAATCTAAA  
TGCCAACTGGGTATTGACACTAGGATAAAGTACAGGTGCTTCAAAATTACATATACAAAG  
TTGAATTTCTCATCTTCTATCTACTCTTACAAAGCTACCTCATTATCCTTTATCCCCTAG  
CTCAGTGAGCATCCCCAGCTGTCAAGCAATATACCTGCTAATCATCCTCAGTTCTTCTTA  
CTCTCTCATCCTCATATCTAATCCCTCACTAAGGCCTGATATTTCAACCTCGTTATTATT  
TTTGGCATTCACCTTTTTTCCATTTTTTGGTTACCAACTTGCTTTCTTGGAATTTTAAAC  
TGTCAGTATTAATCTCTCTGCTTGCAACATAAAGACATATATTTCCACATATTCGCGCT  
AAGTAATCTTTGAAAAATAGTAGTAAGATATTGCCATTCTGTTGCTTAAAACTCTGTCAGT  
AATTTTGTAATTTTCCAACTTCTCCATAGTCTGTAGGACAATATCCAAATGTTTTAACTGA  
ATACACACACACAGAAACACACACACACGCTCACACACATTTTATGATTCATACTTTGAG  
TTTAATTGAAAGATAGAACATCTATAAGATGAAAACAGTTGTAGTCAGAGATTCTGGTAT  
GCAAAGTAGGAGAGAGAGCCAAGAACTAGAGGTATAACTTTGAATTATAATATTGGGTG  
GTCTTCTATAGATGAGACATAAAGTTGTGAGAGTCAATAAGAACAATAAAGAAAGATAA  
TGAAAGAACAAAAGACAAAGTGGATTAAAGACAGATATGCGGTGAAAGAGAAAAGCATTTT  
TACAGAAAAGACCCCCAAAATAAGTTCAATTGCAGGTAGTAAGATGAACAGAAGTCAAATG  
TCTTGGGGAGGATCGGATTGGTTGCTTGTGTATGTTAATTAATGCAAAAGGGTCAAAGAG  
AAGGACTGACTTTATGGCCCTGTAGAAGTCTGAGAACAGGGTCAAAATCCAGATGCATTT  
CTAAGACATCACACTGGGAACGGGGACTTGTAATGAGTTATCTACAAAGTGTAAGAGAT  
GTGGGTAAACAAAAGGTTGTCAATTTCTTCCAAAACAAATTTCTTGGAGTGAAGTGTAA  
CTACAGGTATAGTCAATTAATAGAAGTGCAGACACTAAGACTATGGAACCTTCCGTCTTC  
CTAACCTTCTCCTCAGGCCAGCCTTAAAGGCCTGTGAAGATCTATTAATAACACTGCTGT  
TTTGTCTCTGGCAGCTCTTGGTGCCAGAAGGCTTGGTGCCAATTTGTGGTTGAGCCCT  
CCTTGGGAGAAATCATGCCATTGAGAGACAGCTGATAAGTCAAGCCTATTTTCCCCTTT  
CTTCACTGTATTTTCTGTCTGAAGAAGTGTGTTATGGATTTGATTTCTGTAGAGATAA  
TAATCACAGGATTCAGTGGTATAGCATTCTCTATGCATTTCTCCCTGCACATTTGTGT  
GTGTGAAGATACTCTTTCTAAATCCCTTTCAAGACAAATTATTAATTGTGATATATTAAT  
TATTCTCCACTGTACCTAACGGTTATCAACACTACAGAGGCACCATTGGTTGACAAAAGT  
GAGAGCTTTTCTCAACATTAACATAATGAGCAAGTGGCAATGAGAAAATATTTGTCCAAT  
TAGAGACTTTTATATTTTCTTTTCTTGAGGAAATAAAACCCGAAACACATTTAAGATACA  
TTGCTGTTTGTGCATAGGCGGTAAATTTTTTTTTTTTTTTTTTTTTTTTGAGACGGAGTCT  
CACTCTGTCGCCCAGGCTGGAGCACAGTGGCACGATCTCGGCTCACTGCAACCCCGCCT  
CCCGGGTTCAAGCGATTCTCCCGCCTTAGCCTCCGGAGTAGCTGGGATTACAGGCGCATA  
CCACCATGCCCAGCTAATTTTTGTATTTTTGTAGAGATGGGGTTTCGCCATGTTGGCCAG  
GCCGGTCTTGAACACCTGACCGCGGGTGATCCCCCGCCTCGTTCTCCCAAAGTGCCGGG  
ATTACAGGTGTGAGCCACCGCGCCCGCCAGTAAATAGTTTGAAGTTTTATTTAATCCC  
AGCACTTTGGGAGGCCGAGGCAGGGGGATCACGAGGTGAGAAGATCTAGACCATCCTGGC  
TAACACCGTGAAACCCCGTCTCTACTAAAAATACAAAAAATTAGCCAGGCGCGGTGGCG  
GGCGCCTGTAGTTCCAGCTACTCAGGAGGTGAGGCAGGAGAATGGCGTGAACCCGGGAG  
GCGGAGCTTGCAAGTGAAGCCAGATAGTGCCACTGCAGTTCGGCCTGGACGAAAGAGCGAG  
ACTCCAGCTCAAAAAAAGAGTGTGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAG  
AGATAACCATTGGGTGGCACATTTTCAACACAGATGCACTTCTTAAGAGTCTCCATC  
CGTCAGCGTTGTAAAAAAGGAAGTGGCACGTTTGCATGTAGTTCTTCTGAGACGGAGATT  
TAGGGACAACCTTTGCCAAGGTGTGTAGGTGGAGAATGGGAGATTGAGACAGGCATATTGG  
CTCAGGAAGACAAGGGAGTAAACTAGCAATAGAAAGGAGGGCCAATGCCGTAACAGTGT  
GATGGAGTGAAAACAAGAAAAAGGAAAATGCCTCAGGATTTGGTGGAGAGTTTGTTTTAC  
CTTTTAAAGATAATACTCCTGGTCAGCTTCCCAGGTCTTAAGTCTGGATACTGTAATGA  
TTTTGGATGACTGCATTCCATGACCTGTTTCAAGGTAGGTTTTTTGAAAATAGGAGTTAA  
ATATAGGCTTTCTTCCCTATGTATTAGTTGCGTTTTTTCTTTTTTCAATTTAGAAATGTT  
GTTTTATTTACGTTCTCTTATTTATATTTAATTGAGATGGTGTGGCCATTTTATCCTT  
CTTTTTTTTTGTTTTCTTTTTCTTTTTTATTTTATTATTATTACTTTAAGTTTTATAG  
TACATGTGCACAATGTGCAGGTTAGTTACATATGTATACATGTGCCATGCTGGTGTGCTG  
CACCCATTAACTCGTCATTTAGCATTATGTATATCTCCAATGCTATCCCTCCCCCTCCC  
CCCACCCACAAACAGTCCCCAGAGTGTGATGTTCCCTTCCCTGTGTCCATGTGTTCTCAT  
TGTTCAATTTCCCACCTATGAGTGAGAATATGCGGTGTTGGTTTTTTGTTCTTGCGATAG  
TTTACTGACATTTTATCCTTCTTTAAACATTTATTTCTATCTAGAAAATCCAACCTCAA  
TAAATATACTCAGTTCTACATTATAAAAAAGTATTACAATGAATTTAATGCTTAAACTCA

FIG. 1AA

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TTCCGGAAGTGACGATGGAAGCAGGTTCAAATGCTTTCACTGACACTTTGTGGCAAAGTG  
TGGAACACTACAGTATATTTTTCCAAGTTGTTTCTGATATATTTTTTATGTACATAACAAT  
CAATAAATTGTTATGCTATTTATTTATGTACTTATATGTAAATTAAACAACCAAGAAATC  
GCAAAGTGTTTTATTAAGATGATATCTAAACTGAAATATCACAACCTACTACAAATAATA  
CTTTGTTTCAAAAATAATTTGAATTGCATATAAAAATCACAGTTGCTGTGATTAACATTG  
CATTGATATATTGGAACCTAAGGTTTTTGGAAAAATTGTGTTTTCTTTCAATCTTTAAAA  
AATACCATATTTATAAAAATGAGTCATTAAGATTATCCCTAGGCATTTTCATTCTGTATTG  
AAGGTTTTTGTAGGGACATCATTATTAGTTCAAAGTGTGTTTCACATTTTGTAGTCTGTCT  
TACTATGGCAACTAATTTTTTTTTTTTTTTTTTTTTTTTTTGTGAGAGGGAGCCTCACTCTG  
TCGCCCAGGCTGGAGTGCAGTGGTGAAATCTCGGCTCACTGCAGCCTCCACCTCCCGGGT  
TCAAGCGATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGATTACAGGCTCCCACCACCAA  
GCCAGCTAATTTTTGTATTTTTTAGTAGAGACAGGATTTCACTATGTTGGCCAGTCTGG  
TCTCGAACTCCTGATCTCAGGGATCCACCCACCTCGGCCCTCCCAAAGTGCTGGGATTAC  
AGGCATGAGCCACCCTCCAGTCGGCAACTAATTTTTAAAAATTGTGGTAAAAATATACAT  
AATATACAATTCAACAACCTAATCAGTTTTAAGTGTATAGTTCAATGACATTAAGTATAT  
TCACCTTATAGTGCAACCATCGTCACTATCCACCTCCAGAACATTTAAAATTTTTAAAA  
CTGAAACTCTTCACTCATGGAACAATAATGCCTCCTTCCCCTCTTCTCCTAGCCCCCTGGG  
CAAAAAAAAATCTACTTTCTATCTGTCTGATATGATTGCTCTGAGTACCTCATATAAGT  
GGAATCATGTAATCATTGTCCCTCTCTGTTTTTACCTTATTTAATATAATCAAACTAA  
ATAAATAAGCAAATTTCTTAAATAAAATTGATATATTTAGTACAGATCCTTTTGAGACAC  
TCAGTGGTCCACTAATTATGTACCATATCCAATCACATCACAATATCATAAATTTTATAG  
TCAATTATTAGTTGGCATTTCAGGCCCAAGTATATGTTAATAAGAGACACAATCTTAC  
ATATGCAGTTTACATGTTTTTAATCTAGTCTTAGCACCAGCATATCACCTTAGTTTACAT  
TTGTCTAAGTGCAAGTATTGGTTTTGGAATGTAATTTGCTCATATACAATCTGTAAGAT  
ACTAAAACAAAAGCTAGTTTATTATAAGTGAAATAATGGCAAAGGCCATTTTAAAAATAT  
TGTATTATTTCCCATTTGAAAATCAGTTTAGTCTTTAGCCACAAAATAACAGGAAAAAT  
AACTTAAATCATAAAACTATATCTGAATATTATTTAACATATTTTATAAAGATATCCTT  
CTTTGGATCATGGCTGCAGATGTTTTCATGCAGCTTGAGCCACTTTCCATGTCTTACGGA  
GAATGTGCAGGAGCTATATATCATCAGATTCTTTCAGAGAAAGAACCAGGTAAGACAAATG  
ACATCTGAAAGATAAAGGAAAAAATAATTGATATCTTCTTGGCACCTCTGCATTTCAA  
AAATACTATTTCAATAAAGTCCATGTTAGAGGTGGAATTCAGAATTCAGTGAATCTGCA  
TTCTTGCCCTCTGCTATCCTCTTTTGCCCTCATTGCTCAATTATTCCTCACTCCTGGTT  
AATGAAGGCAGGCTTTTAAATACAGACTAACCATAAATTGACTTTAATATTGGTGTTTAA  
TGTTTATTTCACAGAACTGATTTAAATGTGGTATCAAGTTCAGGTCCTGGGATTTACCAA  
AGTTTCATCAGAGGACACAGTACATGGCGAATTGAGAACCATAGCCTACTTTATGTCTAAG  
AGAATTATGACAAACAGCTAAGTTCTCTGTGAGCTCTCAGATTTCACTCAAAAGAAATGA  
AGAAAGTAAATTCTCTGTTTAGACTTTGTGCTTTTCTCCTTTTAAAGAATTTGCTCA  
TCGGAAAAATATACCATACCAATGGCAGCAACATACTATAAGTTTATGAGCAAATCAATTC  
CATCCATAGTTACTGCAGAAATGTATTATAGGCAGTATTTTTGTTGGGAGAAAAGCAGCAG  
AACTTAGCAAAGTAAGGGAAAAGAGAAAAAGCAGCTTATAATGATAAAGAGCCTTTGTGC  
CCGTAGAGAGATAAGAAAAAATACAAAAGAAATCCATAATGATCCACAATAATTTTAGAA  
TGCAATTTATGGCCATGAAGGGTACAACATGTGATTGGGTATCAAAGAAGAAAGAGTCA  
TGTTAATTTAGGCTAATTAAGAGATATTTTGTGAAGCAGAAAGTTTTTTATTTTGTGTGGT  
TGACCAGTTGATTTTGGACAGTTTGGATACTATTTAATTGGTTAAAAAGCTATTGAAAT  
GGAGTATCAACCATTTCCAGACAGAGGAATGGCATGAGTGATGGTCTGGGCACGGAATAT  
GTTTGACACACAGTGAAATATCAGATTCAGTCTGATGCTCTGTGTATTTTACGGGAAACA  
TTATAAGGGATAAAGGGCAAAAATTCACAGAAACCCAGTTACTATTGGCCATCTGAGAA  
TTTTGTACTGTCCAGGAGAAAAAGAGAGCTCTCATTGAAATGGAAGAGTTAATACAACAAG  
ACATTGTGCTTGTCTGTACTCCTATATATTTTATCCATTAAAGGAATTAATGGATTTTAT  
CCATTTTATGACATTTATTATTTTATGACACTTATCCATTAATGACATTAATGGATAAAA  
CATATAGGAGTACAGACAGGCACAACGCATGGGGAACTATTAGGAGGTCACTGCAATAC  
TCTAGCTAATGGTTACAACAATCTGACATTGGGTATTTGCAATAGGAATAGAAAGAATAT  
AATAGAGGAAAGAGATATTTTGGAGATTTCAAGCATAATTAATGGGAGAAAATGGAAGCT  
TATACTTCAGAGAAGCACAAGTCCAGTGATAAGTTTAAAGTTGATATAAATTTAGTGTGCT  
CTCAGGAGAAGGTGATGTTTACTTTGTACTTTTACAACCTTGACGGGTGAGTGGGTAC  
TGAATAAACAATAAATGTTTGTGTAACACAAATTTAGAGAATGTGCAGTTGTAGATATA  
TATGTAGTTCTGAATAGTCCATTTAAAGACAGATACTAGGTTTTCTTCCAGGGTTTCTAG

FIG. 1AB

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AGTTTCGGGTCTTACATTTAAGTCTTTAATCCATCTTCAGTTGCTATTTGTATATGGTGA  
GAGATATGGGTTTGTCTTCCGCATATGGCTAATCCAATTTTCCCAGCACCATT  
TATTGAGTAAGGCGTCTTCCCCAGTGTCTCTTTTTGTTGAGTTTGTGAAGATAAATTG  
CCTGTAGGTATGTGGTTTTATTTCTGGGTTTTCTATTATGTTCTATTGATCTATATGTCT  
ATTTTTTATACATTAATAGTATCATGCTGTTTGGGTTACTATAGGCTTATAGCATAATTT  
GAAGTCAGTTAATACGATACCCACAGCTTTGTTCAATTTGCTTAAGATTCAATTTGACTAT  
TTGGGCATAGCCACAGTCTTTAAATATTTGAATGGACATAATGTGAAAACCACACTTAAG  
ATATGTTTAAACGGCACAGTAATATTATCTAACACAACTCAAAATTCAAATGTATCCAG  
TTGTCCCAATAGCTTTCTTTATAAATATCTTTTTTCTTTTTATTTCTTCTTAGGATTGA  
AAGGTAAATATCCTAGCATCTACACAAGGGAACCGATGTGTGTGTGTATATATATATATA  
TGATATATATATACACACACACACATAGGAATACATACATGTATATATATACCAGTATA  
CACATAGAATACATAGGAAGATTTTTTATATATATATATATATATATATATATATATA  
TATATATATATATATATCTTCCCCAAAAGTGTGCCTTGGCTTTTAAAAAGCTTACAA  
GATCTCAAACTGTCTTAATAGACTGACAGTAACCAAATCAATCATCCTTCTCATTTGTTGC  
TCTGAGTAGATTGCACCTGGAGAAATGATTGCAGGTATGGATAGCTCACTTAGAGCTATT  
ACTGATAATCTGAAGTGTGTTTCAAGATAAAATAACCAGGGTGATGGGGAATGAAAAGCCC  
ATAAGTTTCACATGATGGATTCTGATTATCTTTAGGCTGGAGAAGCATAGGCTAGGGAAG  
TGGGCATAGCTGTTGTTGTTAAATACTTGAATGAATGCCTTTTTGATTTGAATTGTGTTT  
CTCCAAAAATATATGATTAAAGTCTTAATGATCATTACTCAGAATGTGACCTTATTTGGAA  
ATGGGGTCATTGCAGATGTAATTTGATATGGTAAAGTCATATTGCAGTAGGGTGGGCTT  
TAATCCAATATGACTGGGATCCTTATGAGATGATGGCCATGTGAAGATAGAAACACAGTA  
GAATGTGCATGCACTGACAAAGGCAGAAATTGGAGTTATACTGCACAAGCTAAAGAGCACC  
AAAGATTGCCTGAAAACCACAAGAAAATAGGAAGAGACTAAGAAGAACTTTACTACAGCT  
TTCAGAGACAGGACAGCCCTGCTGACACCTTGATTGAGAGTTCTAGCTCCAGAACTGTG  
AGACAATAAGTTTGATTGTTTTAAGACACCAGGCTTATGGTACTTTTTTACAGCAGCCT  
TAGAAAACAAATACAATGTACATATATAGGTAAAGCTTATTCATTCAAGTTTCCAAAGAAATA  
ATTAGGATCTTGTAAGCAGAAACGAAGGGAAAACAGAACATGAACAAGAACTTGCTAGTA  
ATTAAAGCCACTGCAAAATGAATCAAGGGCTCCAGCAGGTTTTAAATTACCTGGTATTA  
TAAATGTTCAAGCAGGATGAATCAGAGATGGTGCAGAGGTGATTATTCATGCATCAGATG  
GAAGTTAGACTGAATAATCTCCAAGTGAAGAAAATTATATGATCCTATCTTAAAGCCCTG  
TCAAATAGAGGTTGGTAGCTTCTTTTCAATTTTCTGCTTCAATCAAGAGGATATGGAT  
GATATAGCTTGGTGGATAACACTTAAATTGAAGACCTAGTACTTAGTTTTACTTTTACTT  
ACTCTAGTACTTAATTTTTCTTAGGTAGGCCCCCTTAACCTCTCTCTCTCTTATTTTCCCAC  
CTGTTAAACAGAGATATTAATGCTATTCACTTCCCTAGTGTTATTATGATGAACTAGTTA  
ATAATTTAAAAAATGCTTAGAACAAGGCACAGCACATAGTAATGACTAAAGAAAGAAGTG  
CTTTTGAACATATATTGCTCTACTATTGCTCTAGATTGTCTAGATATAATGCATTAAGTC  
TTCCACCAGTGCCATTGCTCGTGCTCCAAATAACAGAGTTAAAGATTAGAAATAATTGC  
ATGTTTTCTAAGAGTCTGCGCATTTTCTTAGATCCAATATTGTACTATTTGGACAATTT  
ATTGACCAAGTACCAGAAATATAATATTTTTTGCCAATTTTCTCATAACAACTGTGATAA  
TGTGTATGTCAACTGCTAGGGTGGGTTTTGTGTGTGTGTGAATATGTGTGTGTGTGTTT  
CAAGTGTTTATAGAAAATAAATCACTCAATGGCATAATTTTCAAATAATAAGACTACAG  
TTACCCCTGATTAAGGTTACCTGAGTTTTGGATATTACCACGTGAGAGTTAGAGGACAAT  
GTGAAGTTTTCAAATTAATCCTCTGAAATCCAGGTATCTTGTAAATTGACATCTGTT  
GGTAGCTGACAGCCAATTTAGCTTCCAGGAAGTAAAGAACATTTTCCAGCTTATGAAA  
CTATTAATAAATGTTACATAATTGTCCAAAGAAATCCTCATTCAAGTGATTCAAATTTAAC  
AAAATTAGGTTTTATTTATTCGCTATGTAAAGATACTAATCCCTGCATTATTTGGGTGCA  
TGGGTGACAGCTCTGACAGGTTTGTGATGCCCCAGACAAATTCAGTAACCTTTCAGTGAAG  
CAAACCCATGAATAGATGTGATGGCAGCGGTACACCTATATAATTCAGAGCTAGTGAT  
TATGTAACTTTTATATACGTGACACCGAAGGAAGACAGAGAATGGAGGAACGGGTGTTT  
TTTCAGTAAAGAGCAACTGAATGAGACAGTACATCTTTTGAAGTGGGGATATACTACAAG  
GCAATGAGGGAGGCTGGCTATGAAAGTATTGAAAAATATGTTTGATTGCTGGGTGATGTT  
TAGAGGCCCTAAGGTAATAGAAAGGAGACAAAATTGAGAGTCTGGAACCTATATGTACTT  
TATTACAGTACTCTCATTTTACCACAAAGGCAACCCATGTGGTGAAAAGACCACAAGC  
ATTGGAGCTAAAGCCAAGTTATAGCTGTAGTTTTATATTTTGTGAGCCCATATGTCTCA  
GACAAGTTTCGTGAGTTAATTTCTTTGCTCAGCTTCTCTTTTATAAAATGTGGGTGA  
TATCATTGTCCCTTAAGATTGTTGTCAGCATTAACAACATAAGTATATGAACCATCTAG  
CTCGGTATTTGGCAATGGTAGGAGCTGAATAATTGTTAGCTCTTACCTTAAAAAATTATT

FIG. 1AC

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TGTTAAAGTTCCAAATGCAGCGTTTCAGGAGAAGATATGGGTCAAGGTCATGGATGAGGC  
AAACACTACAATTCAATAAAAAATTGTTAGTTCTTAATTTATCTTAACCTCAGCAACCGTTT  
CTTGAGACTCTACTACATATTGAGTACTGAGGGAATAGAAAAGATGAATCAAAGACCATTT  
TAAACATCTGGCATTGCAATTCAAAATCAAGTAAAAATAAATACAGCCTTATGATTTA  
TTGAGAAATGTCATGCAAGGTAAATGAACTGATTTTAAGCATGTACTTAGCATTACACA  
GATTGACAGATTTCAGTGAACACACGGCACAGCCTTCAATTATTTTTCTTTTTAAATACAT  
ATTTGTGGACTTTATAGAAATACTGACAGTGTTTCCTCACCAATACCTATTTTTCTTTGTT  
GAGTGACTATTCTTTTTCTTTTCAAATTAGTTTGTGTGGCAGTGTGGAAGAACCACCAC  
ATGAGGACGGTAACCAACTACTTCATAGTCAATCTTCTCTGGCTGATGTGCTCGTGACC  
ATCACCTGCCTTCCAGCCACACTGGTCGTGGATATCACTGAGACCTGGTTTTTTGGACAG  
TCCCTTTGCAAAGTGATTCTTATCTACAGGTAATTGTTTTTAATGCTTTTTTTGAAGCTA  
CTAAAAAGAATGTTTCAGCCATAGCGATGGCCCTTATGGTAAATTAAGTAGTGAGTTGAGA  
AATATATTTGCCTAAGGCATTGACAACTGAAGGAAAAATAACTTGAAGATTTCTGGAG  
AAATAAGTTAAGTTCTGGGTAAAAATTAAGCAATGAACTGCCAAATCATCATTAGATGCT  
GCACAAACATTTTTGCACAACTTTTTTGATTACTAATTTGATTCCAAAAGTTTGATTTTG  
CACAACTTTTTTTATTCCAAATTTGATCCCAAAAGTTTGATTTTGCGCAAACCTTTTTTG  
ATTCCTAATTTCCCATTTGTTAAATAAGAACTGAACCAATTAATGATTTAACCAATTA  
ATGATCTCCCAAACCAATTATTGATCTTCTCTTGAACCAATTAATGATCTGCCAGTCC  
AAGTCATTGAGCATATTTGTTTTTACAAGTGATTTTATTTTATACTGAAGAATTAAGACC  
TACTTGGTCAAATCAGTGCCATGAACAGGTTTTAGTGTAGATTCTAATTCAAACTACCGG  
ATTTGGAATCTCCGTTCTGCCATTACCAATTGTATGCTATCAAGCCAAATAGTTGTAAT  
TCACTTATTTAAAGAATAATTTAAATGAGATCTACCTCATATGGTTGCTGTGACCATTT  
ACTTACATAATTCATATAAATAAGTTGGCACAGTGATTACCCTCTGGAAGAGATGATCTT  
ATAAAAACAGTATATTCTCAATAAACATCAATTATCAGCATCAGAATCATCATTACTAGG  
TGTTTTCTTTCTTAAAGAGTGAAAAACAGCTTCTTTTTCTATTTAATTGCCATTTTCAGTA  
ATTAAGAATGAATACTTTTCAGAGATTAGTGTTCTGATTGTTATTATAGCTCTAAAATTTT  
TGAAACAAAAGATTCATCAGATAATGTTTACATTCACCTCATCCATCCTAAAAGATGGATT  
TCCCTTAGGAATTGGACAGCAAATGAAATGGTGACCACTCTCTGCTTGTCTTCCCATAGC  
TTTCCTGCACCCTCAGTTTTTACGCCATGCAGTCTCCAGATGGTGCCTATAATATTTTA  
AGAAAACAGAAAATAAGCTCCCAGTAACAAAAAATTAGGGAGGGGTCACAAATAGCCTAT  
TACTAGACATTATGCCGATTAGGCTTTTGGAAATGAAATGTTGCAAAGAGATATTTAGTTC  
AATAGTTCCCTTAATCTCTTATAAAAAGAAGTGAAAAATTTTTTAAGGTTAAACATTGT  
TTATAGAATAGTAAGTGGAATAACTATAGAAAGTTATAAGCTCCATGCATATATTATGTT  
TAATTATAAAGCTAGTTTGGATCAGCCTGCTGAAAATCATGAATGGATTACAAAACGAAC  
AGTAGCACATTTTTTTGTGTGTGAGGAAAACTACATGGGACAATAGAGAAAAATATTCT  
CATAGAGGAAAAGTTAGTAAGAAATGAATGGCTCTGGTGGTGTGTCATAGAGGCACTAG  
GAAAGTAATACATTTTCAGATAATTCTAATATTTTATTATCTCTGTGGTACTTCCAGAAAG  
CCTTTTACCTCTCTTGGTTTTCAATAACTACCCAGGAGAATATTTTGAGGATTCTCTTAAG  
TTTTGGGATGGCTGCAGTTGCCAGAATCTTCAACTGACTGGTAACATTTTCATGTTCTCT  
CTGTGAAACAGAAGATTCCCTGGTGGGAAGTGAAGTGATAAGGGCAGGTGCAGTCATGTG  
CTAATGCACAGCGATAGCTTTCTGCAGAGCAGGCATCTCAGAGTTTCTGTGAGTATTTG  
CATTAGAGGACAGAATGGAAGCAGTGTAACCAGTGAGTGATGCAGAGCATGGGTATCTCT  
TATAATCACTTACAGTCTCTTTTACACAGCAGAACTATTTAACAAGTCTTACAGTTCAA  
GGAATATCCTCATCTCTGGAAGGATTCTGTCTGCCTCTCTGCACACAGTGTCGAATCTAA  
TCAATTCCTTAGCTGCTCCTCTCTCCATAGAGCAAGGGAAAAAACTACTGGGTAACCAC  
ATGATGCAAAAGACTAGATCCATTTGTTACCCCATCTAACATTACTTCTTGATGGAAAGG  
TGTAATGCACCAAGAGATTGGTGCACAGGTAACACTAGTATCTCCAAATCTTTCATATT  
TATTGCCTCATTTTTTCATAGAATGTTCCCAATGCAATGAACAGTGCCAATGGGCAATAA  
ACATATAATTTAAATTTGAGCAGATTTTCTCCCTAGTTGTGACATTCTGTAACATAATGAC  
TTATATCCCTGATATGATATTTATGTCTTACTGAATATTTAAAAACATGTTACATCATGC  
CCAGCCACATTTTAAAGTTATTTGGTTGCATTTTAGATTACTTGGACGTTTATTAATTTG  
CTATAATTTATATGTTCTTTTTCTTCTAAATACAATACAGCCTTTAGATTTATGAGTGAT  
ATGCTGTAACGCATTGGCAAATGCACAAAAATCTCAAAAGTCTCACAAATGTTATAAAGC  
TTAGCTGAATAATTAATTAAGTCTTTTGTATCTTTAATAATTGCATAACTCCAAGACCA  
TTAACATGTATTTCAGCTATTTGCTGAACAATTATCATGTATTTCACTTCTCTTCCAACAA  
TGACAAGAGCATTTGGTTACTTTTTTCAGAGTGATTTTTTTTAACTGCAGAAGACGCCCTAC  
ACAGAAAATGCCAGAAAAAAAAGGAAGCCAAGTGAGATGTGGGAGGTGGGCAGTGGGTGGT

FIG. 1AD

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CAAACAAGCTCCCTCTCTTTTCAGTCATACTTTGAAACCTTTCTACCTATTAGTGCTTATC  
ATCCAAATCTGTGATTTGGCAAATTTTCATTTCTCCTTATAGTGAATCTTTAAGATACC  
TTTGCCGTATCTATTTGCTAGTATAAAACAGTGGACTTCTCTACTAAAGGAAATCCCCAA  
ACATTATCCTGTGCGAAGGGTGCCCATAGTATAGGTCAAAGACCAAGTACCTGAAGGCAG  
AAGAAAGTTCCCATTTATCTCACTCCACTTCATTCTCAACATTTCATAATCCACACTAGATT  
CATTTCTCAAATGACTTACTATTCAACAACTTGAGCTAATATCAGAATCCAAATGAAAA  
AGACACCCAGAAGTGCACCTCTTAGAAGTTAAAAGCAACAACAACTTTCACTTATAATT  
ACTTATGATAAAATGCAATTTTACATCACCTCCAAGAAAATCTTATACATTGCACATAAT  
TGTATATTAATGTGTTAATTGCACAAGCAAATATAGTAGGTCAAACAATGAATATTAGCT  
CACTGATTGTCAAGGGTTCATTCAATGGATTGGTTCATTCTACTGTTAGATACATCACAC  
TAGCATATTCCTCCCTTTTCTGTGTGATGAAGGGCAGTGCTCCCTGGGTCACTATTGGCA  
CTGGATGTCAGTCTTCCAAGTGAAGTGAATGATTGATTATTATGACCTAATGGCATT  
GGAAACACTAGAAATGACATTGATATTTGAACCATGCTACATCTATCCCATTTATCCATG  
TTGATTAAATTAATGGATTATAAATTACTAAGGCTTGATGAACACTTTGTACTTCTAATT  
GCTAGAGAGGATTGATATATCTCTAGCCCAGAAGCTATGAAAAGGCGACTGTGCGAATCT  
ATACAACCATAGTTCTATTCAGGTTAGCAATGGTATTGAGGGGCCCTAGGTGCTTAAC  
TTATTTGCAGAGAAGGAATGGAGGTTGTAGAGAATAAGGTGATACTGGTTTTGAGAAAGAG  
AGTTGAAGGTACCCTCAGGTAGCACTAAGAAATTTCTAGGAGTCACTAATCAACTAAGC  
CCATTCTCATAGAGTCCAGCCCTTAAAATTTACACTTAAAATGAAATTAGCCTCCAATA  
TTTAGCAAAGGTTAGGCTTTCACTTGTAATTTCTATGAATATTCTTCTCTGAAAAGCAAT  
CTGTTCCAATTAAAATATAGAAGTTCAGACTCAAGAATGAAAGATAAACTAATAGTATC  
ATCATCATTATTATATTATAATCATAAGAAATAGTAAACACACAGCACTTATATGCCAG  
CCCTGGAATAGACATTTTCATCTCACTAAGTGTCCATACAATTCATGGTTAGGTACTA  
TTAATCATCCACATTTTACAGATGAGAAAAGTGAAGGAGGTTAAATAATCTCCT  
TAAGATCACTCCATATGTCAGATGGGATTTCATGCCAGAAAACCTGGTTGCAGACTCGAT  
TCCAGCTATACTCTCTGCCTCTCCCATAGAGAAACAAAAGAATCATACTTGATAAGAAT  
CTTATCCTGTTGATTACTTCACTTAGCACACACACACACACACACACACACGCAACA  
CACAACACACAACACACACATTAGGCCCTAAAGCTGTAAAGTGAGTGACTCAATAGTGTGC  
AGCTAGCTGATCAGAGAGAGAGAACAGATAGTTCATCCTGACAGCCCAGAGACTTTCTGC  
ACTGTTGCACTGGATCTTAGATCTCTTCACTCATTGTACCTATAATCAACATATCAAC  
AAGAAAGGTCCTCATGTAAAAGACAGAGATAACTACCCTTTCCACATATTATGAGATCAA  
TATAACCAGGACAGAAAAATAGAAGAAGATGACTGGACTATATCTACTGCCTTCAATTAA  
GGCTCACCCTATTAATGGATTAACAAATATTTGTTTTAAAGACACATGCAAGTATACGT  
TCACTGCAGCACTATTCAACAATAACAAAAACGTGGAATCAACCTAAATGCCCATCAATGA  
TAGACTGGATAAAGATAATGTGGTACATATAACCATGGAATACTATGCAACCATAAAAA  
AGAATGAGATCATGTCTTTGACGCAACATGAAAGGTGCTGGAGGCCATTATCCTTAGCA  
AACAAATGCAGGAACAGAAAAGCAAATACTACATGTTCTCATTATATAAATGGGAGCTAAA  
TGATGAGAACACATGGACACATAAAGGGGAACAAACACGCACTGGGGCCTTTTCAGAGGGTA  
GAGGGTGGGAGAAGGGAGAGGATCAGGAAAAATAACCACTGGATACTTGGATTAAATACCT  
GGGTGATGAAATAATCTGTACAGCAAAACACCCATGACAGACATTTATCTATATAACAAAC  
CTGCTCATGTACCCCTGAAATTAATAAGTAAAGTAAACAAATATTTCTTAAATGCAT  
AATGGATATCAAATGTTGTATCAGATATTGGGGACACAGTTGTGAAAAAACAGAGCAG  
TCCCTCCTACCACAGAGCTTTGTTCCAATAGAGAAAAACAGATGATAAATAAGCAAATTA  
GCAAATAATTTACTACATTATACATGCTGAAAGAAAAATAAATAACAATCTGTAAAAAAA  
AATGTAAGAAATCAGAAGTCTTTTTAAAGGGAGAGGGGATTCTGAGAGTGATATCAGA  
ATCAATATTTTCATCCAGTATAAGAGAGCACATTGAACATAATTACATTAACATAAATGT  
GGATATATGAATTTTTAAATTTTTGTTGTTGTTATTTCTTAAAGTGTCAAGTTAAAG  
AATGATTTGTGGCATTGTTAATTATATACAAATTTTGACTGGGTGAAGTTACCTAGTTTT  
TGGAATCACATTGACTAGGCTAGCAGTGAGCAAACTGTCATAAGGAGATTTCGCATACAAA  
ATTCTCTTTTTAATATGACTCGTAACCTTCTTGGGTGCTACATGTTGAAAATGCACTGAT  
GTACAAATAGCCCTTATTATTTGAAAATATGAAATAAGCTACCCATAATTTAAAAATGTT  
AATTAATATAATTTCAATCAAATTTCTATGTGGTAATTTAGAAGAAAGACATATTATTC  
TTTATAATTGAGGCTTTTCCAGTTTGGACTAAACATATGTGTTTTTTTTTCTATATGA  
GGGTATGATTTCTTCCAATCAATGGAAAAATTACAGGACAAAAATTACAGTAATTTAT  
TAAAGAAATGCCATATTATAAATTAAGACATTTGGAGTAAAAAAGATTGCAAAGTTTCA  
TCATACCTTTTCATGTTTAAACAATAAATTTACATTTAAAGTATATTTCTAATATTTTCAT  
TTTTGTGATATAATTTCTTTTTAAATAGAAAGCACTTGATGGATTGTTTATTTTGGCA

FIG. 1AE

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GCTTTGAATTTGCTTATATGTTGTGACTACCTTTCTCATATAGTAAATATATTAAGAGTA  
ATTCTTTTAAACAGCTGGTGCTTCTCTATTACTATGATCTTTCTTTTCTCTAGACCGTGTC  
GGTGTCTGTGTCTGTCTCACACTGAGCTGTATCGCCTTGGATCGGTGGTATGCAATCTG  
TCACCCCTTTGATGTTTAAAGAGCACAGCAAAGCGGGCCCCGTAACAGCATTGTCATCATCTG  
GATTGTCTCCTGCATTATAATGATTCCCTCAGGCCATCGTCATGGAGTGCAGCACCGTGTT  
CCCAGGCTTAGCCAATAAAACCACCTCTTTACGGTGTGTGATGAGCGCTGGGGTGGTAA  
GTACCTTATGGCCCATCAACTGACATTTATATTACAGCAGCAAATTGAAAATTGGATTAG  
CATAGCCATTGTAAAGCTGGGCTTATATATTTTATTGACATTTGTGAATACAGTTTTTGCA  
AGAGCATGAAAACCAACTTGAATTTCAAACAATTTACAGAAATAACTCTACCTATCTGA  
ATCCTTTGGAAATGTTATCTATTATTTTCTCATTTTTCATATCTTTTGGATAGGAAATGAA  
AGGAGATTATTCTACAATTCAGATTTGATTATTTTAGTTTTTCTTAAACTCTTTAAACAA  
AAAGCAATATGGAATACAAATCCGATTATGTATTCTGGAATGATCCACGATTTATAAGAT  
GGTTC AACACTGTGTTGTCTAGTGT CAGGGTCCCTAATGGGCTTCAAATACA ACTGAATT  
TTTTCATTTTAAAGCCATGTCTGGATCACATGGTCCTGGGAACATGGCCAGAGTCAGCA  
TGTGGTTCTCTAAGTCAAATAATCCAAATTTGTTTCTCTATTTCATAATACATTATTGCT  
ACTCGCATAATTATTATCCAGTTTAAAGAATTATATTAATTATGAATCAATCTGGTTTTCCC  
ATCTGACAAGTATGATGTGAAATTTAAGCAATCAGGTTTGAAGGCTTTATGTTTCTTTGG  
TTAGAAATTTCTAGAGTCAGTCTGAGGTTTTTGTGTAACAGTGAGAATACTGCTATCAAC  
ACCTGGTGTAGCACAAATCTGGGCACAGGAAAGAATGACAGAAAATAAAATAACCCTGC  
ATTTCCAGCATAGCATGCACTGATTCCAATATATCATATGAAATATATATTTAAAAA  
CCAATCTGACCTCTTCTAGGTAAGTATACTAAAAATGGCTGATATTTAGAGAATTCATAT  
GTTAACATTGTTTTTTATTAGAAAGATGTATCAAAACAAGCAGTGCACACCAGGGACTGA  
TTAAGGATAATATTCTTAAATATTGTAATCTTTGAATTTCTGTTATTTCTACCTTGGTG  
TTTGTACTAGAACACCGAAAGGAAAAAAGCCAATCACTGATATATTAGGCATATACTAC  
AGGATATATCTACAGCAAGATAATATTTAAGAGAGGCTGGGATTATTTTCATATATTGTTG  
CAAGACCTATAATAACTAAAATTTTATAAATTGCTTTATCTATTACCCCAATATCAAT  
ATCTGTCTTTTATTGGGATTTACTTTTTCTTTTAAACATTCCA ACTTTTTTTGCTGTAT  
TTTTCTCTGTATCATTTTTCAGTTTTTCCAATTTTCCAATTAATAGTGCAGACAAAAA  
AAAATCAATGGAAATTTCCAATGGTAGGAATATTTATGAAGTGTCTTATGTCCCATTC  
ATTTAATGCTCAAACACCACCTTGAGAACTTAGTATATGTCAGGCATTGTGCCACCTGG  
AGAGAAACAGACTCTGCTTACGGGAGCACACTCTATATAATAAGGCTCAAAGGCCAATAA  
ACAAATTTTATAGGGTAATCAGTATTTTAAATATATTTATATACAAATGCTGAGAACAC  
AAATGAGAAACAAACTCAGTTCTGGCCATTTGAACAAAAGTTTACAGAGGAACTGCTAA  
CATTCAGCAGAACATTAAAGATAAGCAAAAATCTCCAGACTGAGAAGAGGGAAAAGGA  
TGTCCAGAAAGCAAGAAAATCCACATCATGGATACTACATTACAAAGCAGAAAGAGTGAA  
TCAGCACTTGTAGTTTTCTGGAACATAGGGGCAGGTAGTGTAATAATTGAATTTTGAAAC  
AAGATGGGTTGGGACTGACTGTGACATGTCTCTTATACGATCCTTTTACACTGGTTTTAT  
ATTTAGAAAGCCTAAAGGTCCTTTCTCAGAAATCCTGTATTAAACTCGAGACTAAATTTA  
ACCTTAGAAAGATTATATTATTTTTTCAAGATTATGAAGCAAATAGGTACATTTAAATCT  
AAAGCTTCCA ACTTGTAAGTTGGGATTCCTTAAGTTTTATAGGGATTGCTATTAGATAAA  
ATATAAAAATATTTTTCAATATGTGTCAGCAGTATTTTCTCTAATATTCCGGCAATTAGT  
TTCACCTTATATGTTTATGGGTTGCTTTTTATAAGCTTTTCTTTTTTAAATGTTTCCCTGAA  
TAATCAAGTAACAGTAACCTCCATTAACAAAAAGATTGCAAAGTCATGGATTCCCTGTTCA  
GTTATTATGATTATGTAAATAGACGTATGATTTTTAAATTACCTCTGAGTGGTAAATATA  
AATACATAAAGCTCATTTCTACTCTGATATTTTATTACATAACTCTAGCATGGACATTTT  
CATTAAAAAAAGGAAACAATTGTTGAATATGTAAAAACCTAACTTAGCCTTCAGAAGTC  
ATTTAAGAAAAC TATTTGAAGGTGATTTTATAATAGCCTATAATTAAATGCTTGTAAGA  
CTAAAATTAAGTATTATTGGACTGAATTGATTAGCTACAAAATCCA ACTTAGTAAAAGCT  
ATACAGTCATTTAAATATTAAATGAAATTGCTAAGAATATTTTTAAGAAAAAATAATTCA  
AGGCAGATTTTTATCTTTCTTATTAGATATTTATTATGATGATTTCTACATAGCATGTAA  
AATCATTGTTTCATGTAACTATTTATAAGTCCATGTTTCGACTTATAATGTTAAACCTTTG  
TATATGTGTGATTGTCACA ACTTTTTAAAAAACCATAGGAAAGTATATTTTACAGTGTCA  
TCTCTCTAAATTC AAATATTTTTTAAAGGCCAACTGTCATTTAGCCTGATTTTTTAAACTA  
TTGTA AAATATCTTCTATTTGAGATTAATTCATAATCTGTGTTTCTTATCTTTATTCTAA  
GTTAAATCAATAATGTAGTTATAAAAGTAGAGAGTAGAATCATAATTATCCTACAACAA  
TGTGGCAGTGGAAAAAATTTGGAAAAGCAATTTGGTCAGTTGATACATATCTATCAAA  
AACTTTTGGAAAAGTTCTGTAAATGCTGTTTTACTCATGGTGCAAAATAACTGAGAACTC

FIG. 1AF

FIG. 1AG



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TATAGAACCAGCCCCAATGCCCATCAATCAATGAGGGAATAAAAAATATGTGGTATGTATA  
TAGCATAGAATACTACTTAGCCATAAAAAAGGAACGAAATAATGGCATTCCCAGCAACCTG  
GAGGGATTTGGAGACCATTATTCTAAGTGAAAGTAATTCAGGAATGGAAAACCAAACAACA  
TATGTTCTCACTCATAAGTGGGAGGATGCAAAGGCATAAGAATGATAAAATGGACTTCAG  
GTACTCAGGGGAAAGTGAGGGAGAGGGGGTGAAGGATAAAAGACCACAGATTGGGTAAAG  
TGTACACTGCATGGGTGATAGATGCACCAAAATCTCAGAAATCACCCTGAAGATTCATG  
TAACCAAACACCAACTGTTTCCCCAAAACCTATCGGAATAAAAAATTAAAAAATACATA  
CATACAAAATTCAGATTCCCGACATAATATATAAATATATATTATATGTTATATATAAT  
ATTATATATAAATATATAATGTATTATAGTTATATATAAATATTATATATAAATATATAAT  
GTATTATATGTTATATATAAATATTACATATAAATATCTATTAATATATATTATTTATATT  
ATATCTAAATATATAATATATAACTTATTATTATATATTATAATATAACTTATATATTAT  
ATATAATATATATAAATATAAATAAATATTATATATATTATATATTTATATATAAATAAAA  
TATGTACTATATTAATATATGAATATATCTAATATTAATATACAATATATAAATTTATAA  
ATATATAATGATTATATATTATATAAATAAATAAATATATATTATGTAGGGAATCTGAAT  
TTATTTATAGTATTTATGTACATATAAGGTAGGGAATATATATATATGTATTAGGTAGG  
GAATATATATATATATATATATATCTTCTAGAGCATTACAAAGTTAGTAATCAATATAA  
TTTAGAAAAGCTAAATATTAACCACAATGCCATGAAGTGATTAATCGACTTATTCGTA  
AGTGTCTAATCTGTGTATGTATCATTTGTGTACATAGGATTAATTATAAATAAAAAATT  
ACTACAGTCCTAGAGGTGTTTATGCTTAATAAGTGAGAAAATATTCATATTGGATTGGAG  
AAAATAAATGTTATAAAGCCTTAAATTTCTCATTTTATTAAAGTATATACATGTATTT  
TTAATAAAAGCATACACACACCACAGACATACTATGCTTAAAGAGGAATTTGTATATGT  
TCCAATAAGTCAACAAAAATAATCATTGTCAAATTTGTATTGTATTTAGTTTTCAAATTT  
TTTTTCACATTTGTATTTGGAGATACAACCTGAGAATAGCCTCCCATTTCTCAGGGAACCT  
ACATTTCTAATAAGGAACAACCAACTGAGTTTATATTTTCTTCCCATTTTAACCAAAGCAT  
TAGTTTTTAGGTTTTTTCATTGATTCATGTCCCTTTTGTAAATAAAAGTTTAGAACAAACCC  
AAATTAATTTTGTAAATTAGCCAGATGTAATCAAGTCAAATAAAGGGCCTTTTAATAACT  
GAACACTTGACTTTGGGTAGCACAAATTAAGAAATAGCTAATGCTTATTTTTCTGAGTAC  
ATTAAGTGAAATTACGACTTCACATTTGGCATGTGTATACCCATATACTGAGTAAATAA  
GTTGTTAAATATTATGAATTATTTTTCCCTTTGCATACATAATATGACAATGAAATCAT  
ATAAAAGGTAAATATGCACTTTGAAGAAAAGCATTGACATGTATCTTTTTTAAAGTCCA  
TCAATTGTAACGTAAGGTTTTGTTGTTTTGACTTTCATCCTAGGTGAAATTTATCCCAAG  
ATGTACCACATCTGTTTCTTCTGGTGACATACATGGCACCCTGTGTCTCATGGTCTTG  
GCTTATCTGCAAATATTTGCAAACCTCTGGTGTGACAGGTATATAGTTTCAAATATTTT  
GCGTGCATTATTCCTCCACACATAATTTGTTATTTGTTATTCCTTCCAAATATTTTGTCT  
GTGCTTTTTTTTTTAGGATGCACTTATAAACAAAATTTAAGAATGCATTGAACCAATATAA  
CATGTTCAATAAAGTATTATATTGTGTGTTCTTTTAAAGTAATGAGAACCCAGACATAGA  
AATATGTCTAGGCATTTTTTAGAGTAATATTAGGAAATGTATTTTATAAACTGATTAAGT  
ACTTTACATTTTTAAATAAAATTTAACATCTGTGATTAAATTGTCTTTTGTCTAGGAATAAC  
ACTAATTTGCTTTCTATGAGAAATAGCAAATAAAAAATTCCTTTAGAGATTTTTGAGACT  
CTAAGTCTGAAAGGTTATATTTGTAATCAGATTTATTTAAACATTGGAACATATAGGTT  
AAATCTCCAACCTCAAAGATCTTATTTTTTAGAATATTATAAGAATCAGGCAGAATGTAT  
AATTTTAAAACTGTATATAATGCTGATTTGGGGTTACTACACTTTGTTAGATAATTCTG  
CTGTATCAGTGAATGTTTGTATTCACTCAGTATTCACTTCCCTGAAATACATATCAT  
GAACTTTTACATACATGTCTCACACAAAAGCTAAAAATTCACTTTTTGGCATTGAGGA  
ATTCATAGTCTAGAGGAGGGGCATCATCAGATGCAGGGCGAAAATTACTTTAAATATAAG  
CACAGAGAATCAGAGCAAAATGTACTAAAACCATATCTAATACAGGAAAGGTAACATTTA  
ACTTAAACCTTGATGATTTGAAGGATATTACCAACAAACACATTTAGTGGTTTTGTAAGAT  
AGAGACAAAAGGATATGGCTCAGTCTCTCCCATTTTGTAAAATGTATCTTAAATGCCA  
CAATTTCTAGAGATGATTTCTCTCGTTCTCTAACTTACTGCCGATACCTTACTTTTATCA  
GGCTTGTGGAAGGACATGCCATTAGTCTGTTTTCTCTGACACATTTTATCCAACCTGAAAA  
GATTTACTGGAGTCACCTTAATTCATTAAAAAGATTTACAAACACTTTATTTGGTCTTT  
GAGGATGTGTCTTTGTTTTTTTTAATCAACACTTGTTATTCAAAGCATTTTTTCAAGATCAT  
CTTTCACCTGACTGGATATGAGCAACACTCATTTTTTTTTAACACTATATGGCTCATAATTT  
CAATATTTTCTCTTTTCTCTGCTATTACAAAGAAGTCATTTCTTTTATGACCTTACAAG  
TGAAACCTAGTAGCAACATTTATTAACATTTTGTTCCTCATTTTTTACTATAAAAACT  
AATGTGGACCAGTATAAATATGAGTGGTGATTTTCTAGATGTTGGTGACAGTTTTCTCA  
GCACTCTCCACCTCCCTATGAAGCCAATGCTTATATTTAGGGTGTGTGTTACTGCAGCA

FIG. 1AH



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TCCTGCTTCCTAGTACCTATTATTGTATCTGTCAGGTTTTGCTAGGTTATTATTCTTCTA  
TTAAAAAATGTGGTTTTGCAACAACAGTTCTGTTTCACTCCTATTACAGGTCAGTGGGGAG  
GGCTGGCTGGGGCACTGTGCTCCATTTGTTTTCTCATTCAGAACCTAGTCTGAAGAAAT  
GGCACTTTCTGGGACATGGCATTCTGAGACTGAGAGAAAAAGAAAAGTGAAGAAAAGTA  
TATTTTCTTTTAAATGTCTTTTATGAACCGGCATGTGTTACATCTCACTTTTTCATTGGCTA  
AAACAAGTCACGTGGTTAAACTTGATCATGAAGAGGGGACACATTCTTCTCTGACAGAAA  
GACATCACACATCACAGGGTAATGGGGAGCTTCTTACAAGCTGGGGATGAATGATCTGGA  
ATGATACACTATACAGAAGTCAAAAACACAAGGGCCAGACTGCATGAATTTAAATCCTGA  
CTCCACCAAGTAGTAGTGACATGAATTTTGTAAATGGCTTAAATTTTTGTGACTCCCTTT  
ATTAACTTTAAATGGGGTTGTATAGCATCTTCTCATAGGTTTGGTACATGCATTTCAGG  
TGTGTCCAAGGGAGAGAACACCGTCTGTTGGGTTCTCAGTTTCTATTTCTATTTGGGCCAGT  
AAAACCCCTTCTATCCCTCTTTTCTGCTTATTACTAGAGACAGAACTAAAAACCAGGG  
CTTCAGGCTGCTAAAAGCCTAAAACAAAACAAAACAAAACCTACAACAACAAAATAAGGTG  
GGTTGGACAAGCTTGCTTAGATGAATTAACCTCAAGTGCCTAAATATAGACAGTGCCTATT  
AAACAAAATATCTTAATGGATGTTGTTTAAATAATGGCCTCTCAACTAATTGTACTTACAT  
TTAAATAGCAAGCATGTGTTGAATTGGTATATGTGACTATTTTTTAAAAAATGCACATTG  
AAATACCAGTATGGTGTCTTCTATTTGTCTGGTCTTCTACTCTACTAAGATAAAGATAG  
TCTCGCTGTCATCTTTGTATCCCTATAAATAGCACGTGCTCAGCACACATCAGTTGCTTT  
TTTCATAAGAACAAGTGAGTAGAATAGGAGAAAGTGCTGGGAAAGTTTAGAGAGGACAT  
AGAGAAATCTATTGCCAGTTACTCCGATAAACATTTGTAGAAATGGATTAGAATCTGAAA  
AATTTCTTGAAGGGGAAAAAGCAATTAATGAGCATGTAGGAATAAAGATATTTTAGATTT  
AGATTCAGATTTTGTGGGGAATGTTTCAGTGTTAAGATTATCCCCTATTTCTTATTTTT  
ACTAGTTAGTGTGCATTGTATAAAAGGTATGCTTATAATTTCTTATTCATTTATTTACAA  
ATTGACATACCTTTAAACTCTTTCAAGGTTGCAATGTATCTGTCTTGTTACTTTTACAT  
GGTAAACTTTTACCATGATACCATGGTTACCCTAAAGTTTACATGGTACCATCAGAGAAA  
ATGTTTTAAAAAGTTTGTAAATGAATGAGTGACACCAAAATCCAAACATTTTAAATTTT  
CACCATTTAAGCATATAGTTTGACATTTCCCAAACTCTAAAATAAATTTTAAAAATAAATT  
GCATCACAGATTCATAAATAATCCACATTCTTTTCATGAATTATCCTCATTAGTACAAGC  
CACATGATTCAGAAGATTTGCAGTAAATGCTTGGGCTGTGAAACTAAAGTCATTTACAA  
AACAGATTGGAATGGAAAATACCAAGTTCAGCTGAACTCACTTTAGCAGCCACAATAAAG  
TGAATTAACCCCAAATGCGTGATTACATAGAATTCTGCTTGAGCAACTCTCAATTTCCAA  
CTGTTAGTGTCTATAAACAAAGTTGTAAGGCATTATGCGTGCCATAGGCTACATCAAGTG  
AGCCATCAAATGAAGAGCTTGTCTTATTTGCTTAAAAATTACAGAGATGCATGAAATCTGT  
TATGTACTTTTGAATTAGTAAGTGTAAGATTATTAGTGAGCAAATTGTGTGTCCTTGTCT  
GACTTTCTCAAGAAGTTTAAAGCCTCATTAAAGAATTAGCTAATGCATTGCTGTGAACTA  
CTTAAATCTCTCTCTCTCTGTTTTTTTTTTTTTTTTTTGGCAATTCGACTCAGAGTACTC  
AGGAAATTTCTACAGATTATTTGCTAAACTTATTTTTTTTAAAGAACTTAGCTTGCTTGAC  
CTTTTCAATTTATCTGTGAGCATTTTTTTCTAGTTTCAAGCCCTTCATATAATTCAACACTAA  
ATCTTAATCGTCATGTGCTTGTGTTAATTTATTTTACATTTATTAAGCACGTACTCTGTG  
TCAGCTATGGTGTGAGGTACTGAGGATGGACTGTAATAGATATTTGGGTCTGAACTATA  
GTTCAAGCTTCTCAGGGCCTTTGAAAGACCTTCTTGTTCAGCTCTTATCACAAAGTTTT  
CTGCTGCTCTTTATTTCAGCACTCTTCTAAGGGAACCTAAGATAAATAATTTTGATGATG  
ACAAATCAGTCTAGTGTGAGAAAATAGGCAGCAAAACAAATTACAATTGCAGGGGCAGAAT  
CAGGAAGGCAGTAACCTCGAGTCCATACAAAAAAAATAAGGAGCACCAGTAAAGGTAAC  
ACATAGGTAAATACTGTAGACAGAATAAACATATTTATCTTCTGTTATCTGATGTAAAGA  
ACAACTGCATAAAATAATAGCTATAAAATTGTGAAGATTCACCTTATAATGTATACAGAT  
GTAGTTCAAAAAGGAGGAGGAAATGGAGCTGTATTGGAGCAAATTTGTTTTATACTATT  
GAAATTACATTGGCATAATCTAAGCAGCTTGTTTAGATTAAAGTTGCTAATTTTAAATTCCT  
GGTGTAAACCACTAAGAAAATAATTTTTTGAAGAATGTAGAAATATAGGTAAAGTAACAAA  
AGAAATTAATAATAGTATACAGAAAATATTTAACACAAAATAAGCAGTAGTGAGGAAATAG  
AGGAAGACAAGAGATACAATATATATAAGTCACAAATAGTAAATGGCAGATATATATTA  
TATTTTCTTAATAATTAGATTAAATGTAAATGGATACAATACTTCAATCAAAGGGCATAG  
ATTGACATAATAGATAAAAACCAACCAATAATTTAAAAAAACCCATGATCCAACCTTTATG  
CTGTCTACAAAGACATACCTTGTATTGAGATATACAAATAGGTTAAATGTAAAATAACA  
GAAGAAGTACTAAAATAATCACAAAAGGGAGTTAATGTGGTTATATACTAAAATTAGACAA  
AATAAATTTTAAACAAAATATTACTATACATAGAGAGGGACATTTTATAATGATGATGGAG  
TTGATCCATCAGGAAGATATAAAAGTTGTAAACATACATGCATTTAGCCACTGAAACCCA

FIG. 1AI

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AAATATACCAAGCAAAAAGTAGTAGAATTAAGGAGACAAGTAGGCAGCTAGACAATTATA  
GTTGAAAATGTTAATACTCACTTGCAGTAATGGATAGAAAACACAGGCAGGGTGCGGTGG  
CTCACCCCTGTAATCCCAGCACTTTGGGAGGCTGAGGCGGGTGGATCACGAGGTGAGAAG  
ATTGAGACCATCCTAGCTAACATGGTGAAACCTCGTCTCTACTAAAGATACAAAAATTA  
GCCGGGTGAGGTGGGGGGCACCTGTAGTCCTAGCTGCTCAGGAGGCTGAGGCAGGAGAAT  
GGCGTGAACCCGGGGGGTGGAGCCTGCAGTGAACAGAGATCGTGCCACTGCACTCCAGCC  
TGGGCAACAGCAAGACTCCGTCTCAAAAAAAAAAAAAAAAAAGAAATAAAGAAAAAACAG  
GCAGAATAGCAACAAGGAAATAAAAGATTTAAACAACTATGAAACCACTGGGCTTAACA  
GATATTTTAGAACACTCCACCAAAAACAGAAGAATGCATATTTATCCATTTGCACATAA  
AACATTTTCCAGGTTTTCTGACTAAAGTCAGAAACAAGACAAGTATGTCTGCTACAACCA  
TTTTCATTTCAATGTTGAACAGAACTGATTCTTTTCAGGGCAAACAGGCAAGAGATAATAT  
TAACAATAATAAAAAATAAAAGGCATGACGATCACAAAATAAGAGGTAAACTATTTCTAC  
TTGTAGGTTATGTGATATTTATATAGAAAATCCTAACGAATTATTTTGCAAAAAATAC  
ATTAGAACAAATAAGTTGAGTTCAGCTAGTTTTCAGGATGAAAGATTAATATATATACAAA  
AATCAATTTTCATTTTATACATTAGCAAAATAAAAAATTTAAATGAAATTAACAAAAATA  
ATTTAAATAGCATCAAAATTAATCAAATACCTAGAAGTAGATTTAATAAAAGAAGCTTAA  
TAAGAGACTTCATCCAGGCTTGATTGCTTATGCCTGTAATCTCAACACTTTTGGGAGACT  
GAGGCGGGAGGATCACATGAGGCCAGGAGATCAAGACCAGCATAGTCAACGTGGTGAAAC  
CATGTTTCTACTAAAAACACAAAAATGAGCCAGGCATGGTGGTGCAGTGCAAGACTATAA  
TCCAGCTACTCAGGAAGCTGAGGCATGAGAATCATTTGAGCCTCAGAGGTGGAGGCTGC  
AGTGAGCTAAGACTGCACCACTGCACTCCAGCCTGTGTGGCAGAGTTAGACTCTTGTCAA  
AACAAAAAAATTTCTTCAGCATAAACATGTATATTTAGGGAATGTCCAGAAATTATAGAG  
ACATGGATTCCATGCAGCAGTTATAATTCCTAAAAAGAGAATTATGAATTCAGTGTATT  
GCTGAGGATTCTAACATAACCACCAAAGATCCAGGGAGAAAATTACCCTATTTTTGTATT  
TAAAAGATGCATTTATTAAATGATGTGGTACTAGTCTCTATATAGGCAACAAAAATAAT  
GAAAAGGAAATAGCTCTGGATTATTAATAAATAAATAGTCTGTTAATCAAATCAATTAAT  
AGATAATGTTCTTCAACATTTTCAAGTCTTATACATGAATATCATTTACAATCATAATT  
ATTAGCAACTTCAATGAGTAGGCCACAGTTATACAAGTTTCTTGAGTCAGTTTGGAACTA  
TTTCCATTCAAGCAACATATAGTCCATTTCTGTAACATTTTGTCTCCATCATTATATTC  
AGTCTCAGAAAGGTTACCAACACAGTCTTGAATCATATGTAGTACAGGTAAAGCATCTC  
TAATCCCAAAACCTAAAATTCTAGCTGCTCTAAAAATCCAAACTTTTGAGAGCTAACATG  
ATGCCAGAAAGTGAAAAGTCCCTGCTATCTCATGTGACAGGTGCTGTCAAAAGTCAACA  
AAAACCTTTGTTTCATGCCCAAATTTATTAATAATGTTATATAAATTTGTTTAAAGACTAT  
TTGTATTGGGTGTTTATAAAATGTAAGTAAGTTTGGGTTTAGACTTAAGTCACATCTAC  
AAGATATCTTTTTATGTATATGAAAATAATCCAAAATCCAAAAAACTCACATCTGAAAC  
ACTTTTGGTCTCAAGAATTTAGATAAGGGATATCAATCGGTACACAACATATACACCT  
ACAATTACAAAATATCATTGAAAAAATTAAGAAGGACTACCTAAATTAAGATATTC  
TGTTTTATGGATTGGAAGATTCAATCTTGTTAAAAATAGAAATAATCTTCAAATTAATCC  
ATGAATTCAATACAATTCCTATGAAAATCCAGATGGCTTTGTATTTTGACACAAATTG  
ACAACTGATCCTAATATTAATGTGGAATGCAAGGGATAGAGAAGAGCCAAAATAATCC  
TGAAAAAGAAATGGAAGAACTTACTTCTAATGTCAAATCTTAACAAAAAGCCACAGTAAC  
TAAGACGGTGTGGTACTTCCATACAGTTAGTCATATAGATCAGTGGAATAGAATTCATGG  
TCCAGAAATAAATCATATTTATGATTAATTGAGTATTGATAAAGGTTTTAACACAGTTC  
AATGGCAAAATCATAGTCTTGACAACAAATGGTGTAAAGACAATTGTATATCCACAAGC  
AAAAGGATGGAGTTGAACCTCACCTCACACCACATTCAAAACCTTAACCTCAAATGAATCA  
TAGATTTATATGTAAGAGCTAATCTCTTAGAAGAAAACACAGAAGAAAATCATCATGACC  
TTGGCTTAACCAATAGGTTCTAAATATAACACCAAAACCAAAAGCAACAAATGACAATGT  
AGATACATTAGACATTATCAAAACAAAACTTTTGTGCTTCAAACCTGCACCATTAACAA  
GTTAAAAGTCAGCCCATATAAATGCAGAAAATATTGCAAATCATATATGTGTTAAGGAA  
TTGTATCCAGAATATACAAAGAACTCTTATGAATTAATAATTTAAAAAATTACAAGTA  
GGCAAAGACTTGAATAAACAATTCTGCAAGAAGATATACAAATGGTCAATAAGCACATA  
AGAAGGTGCTTAACATCATTACTCATTAGAGAAATATTAATCAAATCATGAGATACCTA  
TTCACACTCAACAGGATAGATTTGTTTTAAAGGCTGTAATCATTATTGGTAAGGATGTG  
GAGTAATTGGAATCCTTCTACATTGTTGGTGGGAATGCAAAACGATGTAAGTCTTTGGA  
AACAAGTTTGGTAGTTTCTTAAATCTTAGAGAATTACCACATTACCCACTAATTCATC  
TCTAGTTATAGACCCAGAGAACTGAAGACATGTTTACACAAAACTTACACATGAATGTT  
CATAACAGCATATAATTCATAGTAGCCAAAAAGTGGAACAACCCCAATGTTATCAATGA

FIG. 1AJ

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GTAAATGGAATAACTCATTGTTCTATATGCAAGCAATAAAATATTATTTCAGCTACTAAAA  
GAAATGAAGCACTGATATATGCCACAAGATTGATGAATCTTGAAAACATACTAAGTGAAA  
GAAGCCAGGCACAGAAGGCCACATATTACATAATTCTATTTGCATGAAAATGTTGAGAAT  
AGGCCAAATATATAGAGCCAAAATAATTTGTCCTTGGCACGGGCTGGCAGAATGGGACAAT  
GAGAAGTGACTGCTAATGGATTTGGAGCCTCATTGGAGGTGATGAAAATGTTCTAGATT  
AGTTAGTGATGATGTGATAGTTGCACAACCTCTGTGAATATTCTAAAAATCATTTTTTGAA  
CCCTTAAAGCAGTGAGGTTTATGGTATGTGAATTATATCGCAATAAAATGTTTTCTTTT  
AAAAAGAAAGAACAAAAATGATGGGATATTTTAAATTTTAAAAATTGAAGACTTTTTTT  
TTTTTAGAAAGTTCTGCTGCTGAAACCACAGGGAAGCAAAAAAGGTTGAACACACAATT  
TGACATGTTAATGTAATGAGAGACTATAATAGGAATTATCCACGGGTTGTTTTATCTGTA  
CTTCTGACTAAAGTTTTTTCCGTACTTCTATAGACTTTAAATGGTCCATAGATGTGC  
AAAAATGAGAGAACCTATTCCATGAAACCATATATCAAGTCCCAGAGAGCAGAGGGAAA  
ACCTTTTTTTTTTTTTTTTTTGGCAAAGAAGAAGTCATAGACTGTGTGAAAGAATAATGT  
TGCGAGACAACAGATCTGGAGTTGGACAGGGGCAGGAGGCATAGTGAGAAGATCAGTTAT  
TGCAGTTGTCATCCATAAGGGCCATCTGTACACTCTGAAAGTGGAGCTATTCATAGTGAG  
AATGATGTTAAGAAAAGGAACAAATAAAATTACAGTCCTCGTTATAAGAATTTAGCATGC  
AAATCTTATCAGAGCAGTACTGAGGTAAACAAAAAGTGTCAAGAAATCATGGGATTTAAT  
GTGAAAACTCCCTCAGTGTGGAATACAGTCATCTTCATATGGTGGTGGGTGTAAGGGG  
CAAGGAAAAATTTTCATGGTCCCTGCTGAACAGGGAATGTAAGGGGATTATTGTTTCATA  
GAAGACCGCCAGTGCCCTACCAATATCTGTTATACTCTATTATGATGAAATGGGTAATAG  
GTTAAGGAATACCATAAGGGGAAAGGAGACTTGTCTACAAGTTTCTTAGCACTTAGCAA  
ATGGAGCAGGCATTTGCTATGCATTAATAAATAAGCATCATCCAACTCTCAGACTCATC  
CAGCCACAACTTAACTTTTTGTTCCCTCCTCCTCCAGATAAAATTTCTCGACTTATTTCC  
ATTTGTCATCTTTTCTCACTAACCGCCACCTCCACTGATGTCTCAGCCCACTTCAGTGT  
AGCTTCAGCTTTTCATCATTACAGTGAACAGCTTACATGAAAGTTACCAATGATTTCATA  
AGAATATATATTTTTAAAGTTTATTTATTGATCTTTTGGCAGCATTAAGCAATGTTGTTT  
GTGGTTTCATTGCTCATATACTTTCTTCTACTTTGATTTGAATACTTTTTGCTTTGAAT  
ACTTACCTTTCCCTGACCAGTAAATGCCACTTTGCTAGGTCTCTTCACAGCTCCAT  
GCTTTTTTTCAGGTAGTCCCTTGCCAGGTACTTTTTAAGTGAGGTGAGTATCAAATATA  
TATACACATCAGACTAGTCCTCTGGGATACACACAATCACAAATACACTTAAACACTCAA  
TGTACCTTTATTATAAAATCTTGAAATGAGTTTTTATAAGTCTTGCAACCAAAGTTTAAAA  
AAGAATAAATTCTTTTTTAAATTTGCTTTGGCTATTCCAGGTCTTTTGCACCTTTCATAAA  
AAATTAAATTTAGTACTTTCATTTCCAGAAAAAAGACTGTCGTGGTATTGAACGTGATTA  
ATTGCATTAACTCTATAGATCAATTTGGGGAGAATTGCCATATTAACAATACTAAGCCTT  
TTAATGCATGTCCACAATGAATATATTTATTTAGGAGTTCTTTATTATCTCTCTGCAATG  
TTTCATCATTTTTCAGTATATATATATATATAATGAAATATATATACTTATACATATATTT  
TATGAAATATATATACTTATATATATATATTTTATGAAATATATATACTTATATATATATTT  
TATGAAATATATATACTTATATATATATTTTATGAAATATATATACTTATATATATATTT  
TATGAAATGTATGCCTAAACACATTCTTTGATATTGAACTTTTAAATTTAATTTTC  
CATTTATTGCTAGTATGTAGAAGTATAATTGATTTTTTTGTTATTGATTTAATGACCTG  
CTCCTTGCTAAATTCTTTTATAAGTTCTAGTGGGTTTTTGGTAGATTCTTTAGGATGATC  
TTTGTAAAGCAATAAATTTCTTCTCAATAGAACCAATCTGTAGGCATTTTATTTATTTTCT  
TTTCTTCTTGATTGGCTCAAAGTCCAGTACAATGTTGAGTACGAGTGGTGAGAGAAGAC  
TTGATTTTTTTGAGTGGTAAGCCAACACTGCATTGCTAGAATAAATCTGATTGAGCAAATG  
GTATTATCCTATTTATATATTGCAGGATTTAATTTGATAACATATTTTTAAAGAGATTTT  
TATCTCTATTATGAAGGATATTTAGTTGTTAGCTGTCTTTTGTGCCATATCTTTGATT  
ACAAAGATAAATGTGACCTCATGAAATTTGTTGGAACATATATATTTCTGTACATTTT  
ATTAAGTCTGAACAAGATTGGAATTATTTATGAAATATATATACTTATGATTGAATTCATTAA  
TGGACCTATCTGGGCCTGGAGATTTTCTTGTAGCATAGTTTGTAAGTACAGAGTCAGTTT  
TGGTCATCTTTGTCTCTCAAGGGCTTTGTCCATTTTCATGTAAGTTGGCAAATTCATTGTT  
TATCCATAATGTTTTTAATGTTTGTAGCATGTTTGCCCTCTTCTCATACTTTATCCTGG  
TCACAAACATTTTTTAAGACAGAGTAGGTTTTAAGGTCCATCATGTACATGCTATTTCCA  
ATTTCATACTGTGGTAATACATTTTTTCAGGGTGTATTTTTGCATTAAATATGATTTATAA  
AGTTTATTCATAATAGTGAAATAAAAGTGGGGTGCATGTATTTTACTTAATCCTTCTCAG  
TGCCTGCTTGATTGAAACCTCTGAGATTTACAATAATGTACTTTTAGGGATGCATTAAGG  
ATTACTAGTGCATAGTTCTGGAGCTCAGTAATGTGAGTTATTCTCTTAATTTTATACG  
GAGTTTCTCTGAATTCTCCATGTCTCTAGACAGCTTATCAATGGAGAAATTTATGTGTCC

FIG. 1AK

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TCAAAATGAATGCAGGATTTCAGCATCTTCTATCCTTATTTAGATCATTATCTAAAAAGGG  
CATCACTACATTTTTTTTTTCCCGATTTTCAGGGACCATAGCTTTCTCTTTATGAAAACGT  
ATTTTTTTTTTTTTTTTTGAGATGGAGTTTGTCTTGTGTTGCCAGGCTGGAGTGTAATT  
GTGTGATCTCATCGGCTCATTGCAACATCCACCTCCTGGGTTCAAGCGATTCTCCTGCCT  
CAGCCTCCTGAGTAGCTGGGATTACAGGCATGTGCCACCACGCCAGCTAATTTTGTATT  
TTTAGTAGAGGCGGGGTTTCTTCATGTTGGTCAGGCTGGTCATGAACTCCCAACCTCAGG  
TGACCGAAAACGTGTTCTAATGGCGGCAGAAGTCATCAGATGCAGAATGTAGATTCTCTC  
CTTCAGGGGAACAGTCAGTGATAGAATCACTAAAATTTAATTGATCTATCAGAGATCATT  
TAGAAGACAGACAGTTCAAGATCATTTAGCAGACACATACAGGCTTTTCATGATAGGAGT  
CTCCTGGAACATTCCAGCATCCATTGCTCATTCTTTTCAGTTATTTTTTAAAATTGCTTT  
TTAAAATGAGAGTCACAGAAGAGAAAAGTTCCATCTCTCCCCAACAGTGGGTTAAAAGA  
TTGAGTTGAACCACTACTATGTAAAAAGATTGTCTACATGACAAGACATACAGAGTGAG  
AAGAAAAATAATTTATCCGATATTTCCATTCAAGGGCAGGTCTTTGTAAACATCATTG  
CCTCTTCAAGAAAAGAAAATGGTCAAAGGAAATGTCATATTAATTTATCTGTGTGGACATA  
TAAGTAAAAATTCGTCTCAAATTAAGATTATCGAACAGACTTTGATCTGGTGGTGTAA  
AAATCAACAAAATCTATCGAACATCTATTCTGAGAAACCACAAGGACACATTGGTCAGTA  
CTGGTTTGCCGCACAGAGACAGAAAAGTAAAAGCTGAATAATCTTAACAGAGCTAAGGTGG  
CCTTTTCTGTGTTTGTGGCACATTTTCTCTTTAAAAAATTATGCATGCTGAATTTTA  
TTGTCTGTTCATAAACCTTATCAATCTTCATGAGCTTACAATTAAGAGAATATTGTAC  
TTGGAGGGATTCCCTGCTATTATCAAATAACTTTGAAAAGAAATGGAAGGTACAAGTTG  
TGTAATTACTGTTACAAATTCAGCTATTTGAAATATTAATGTAAGACCGCAAAAAATCC  
TCAATGGGTTTGTGTGCATTTTAAAGGGCTGGACCACAAAACCTGATTTCAAACAATTTCA  
TAACTACAAATAGTGAACAACAAAAAATACCTTGATTTTTTAAAAATATCCTTTTCATTCAA  
AGGTTTGTCTTGTCCGAACCTCGAGAAGCAGAAAACCTGAAAAGCTACAGGTAGTTAAGTT  
CTATCTCTCGGCAGCAGATGGCAGTATTGATGCGTGAATAATCCATAACAGGTTGCTTG  
ACGTTACTTGTCTGGGTTTCTCTGCTTTAAACTTTGGTATCTGAGCTGAACAAAAATTC  
CTAATAAGATAATATGGCTGACATCCCTTTATCATTCTCCTTTCCCAAGCTTTGTTCTTT  
TTACAAGGAAATATCTTTCCACTTGCAGCTTTCTTTAGACATTGACAAAATTTTGTATGT  
TTTAACTTTTTTTTCCACACAACTCCTATTTGGTATTTCGTCTGAATTAACGCCAAGCAC  
ATACTAAGGTCAGCAAAATGCTCTGGAGAAACAGGCGCTCAAACCTCCCACACCTCAGGCG  
TCTGGAAGCCTTTCTTACTGTGTTTCTAATTACTTCCCCAAAGTGGAACCTTTCTTAAG  
TCAAATTGCAATAAGGGTCTGTCTCTTCTCCTTTCAGATCCCTGGAACATCATCTGTAGT  
TCAGAGAAAATGGAAGCCCTGCAGCCTGTTTCACAGCCTCGAGGGCCAGGACAGCCAAC  
GAAGTCCCGGATGAGCGCTGTGGCGGCTGAAATAAAGCAGATCCGAGCCAGAAGGAAAAC  
AGCCCGGATGTTGATGGTTGTGCTTTTGGTATTTGCAATTTGCTATCTACCAATTAGCAT  
CCTCAATGTGCTAAAGAGGTAAAACCTTATCTGTTATTTGAAAATGAAATAGCCTGCCTTT  
TCTTGATTCTTAATTAACCTTTTTTTTTTTTTTTTAACTAAGCCAGAGAAAAATCTAACT  
TTCTGCTTAGATACCTTGTGAGCCAGATGACTCAGTTATGTTGTTACCAGCAGGTAAGG  
CGAACAGCCTTTAAGAGTGCTCAGACATGTGCTTTTGTGATGCGTATTCTCAGTTGCATG  
GCAGACATAAAACAGATGTTTCTCAATCTCTTCAAGCTAGTTGCTAAACCTTAGATGCA  
GACAAAGTTCTAATGCGTAACAACCTCATTTACAGCTTGCAAGTTCTTTCTTGATGAGAACA  
AACGGGTTTTTCAAACTTCGTTTCCAAAAACATAGGCAATTGTGAGAGAATTATATCTT  
AAGGATAAAAAGAGATAAAGAACCTTATGTTAGTATTCTAATTATACTTAAAAGTGCAATTG  
GCGAGCACTTTTTAAAAAAGCCATCAAGGCAGATATGTATGTGCAATGTCTAAACAGAA  
GAATTCATTTCTGAAGTCACTGAATGAAGCTCAGGGCAGATAGTAATAAAAAATCAATGA  
GGGAAAGTATGCTATTTGCTACAATGCAGGCACAACCTATTAAGTTAAAAATTTTGACCCA  
TGACATGAGCAGCAGATGCAGAGGCAGTGGTACACACTAACTTCATGGCCAGCCAACCTT  
TATTGGGAATTATCGAACTGTTCCACATAGACTGGTCCCAAGGCAATACCAATTCTTGT  
TTACAACAGGCTTCGAACCTTAAGCTAGAATTGCTCCTCTCACTTTGGCCTGATTCAGAAT  
CAATATTATATCTCTCACAGCTGGGAACCTCTGAAGAACAGCAGCTTTGGCTGGAGTCAGA  
AGAAGTGGTATAATCAGCCGCAAGGGTTCTCATTCTCTTTGGCCCCCTGTTTTTGTATGGT  
TTAACGGCTTTTTCAATGGAGAAGAAATGGAGAACAACTTCTGTTCAAGTACTATTTT  
ACTACAGTCACAGCCTTAAAGATATATGATTTTTTTTTTGTGGCCTGGGTCTTGAGACATA  
TGCCAGCTCACAAGAAAATAGAAATTATTTGCCCTCCATATCTTTTTGTGCTTTGCTTC  
TTATTAATTATTATTATTATTATTATTATTATTATTATTATTATTATTATTATTATTATT  
TATTATGGCCACCTGCTAGATACTCTCTCTGCTTTTAAAGAACTTTATAAACATGTTATG  
TTACTGGATGGGTTTTATTCTTTCTTTCTTTCTAATCTTTTTTCTCTTTTAGTCAGTC

FIG. 1AL

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TAAATTC AATGAAAATTGGATTACCTCTCTCTGGGTTACGTATTTGGATTTCCTGTATC  
TCAGAACTTGCTCTTTCTTTTATTTCCAAGTACTTTTTTTGTCAATAATATATGTCTTA  
TTCTTCTGACTCAAATCCCTTCTTTCCAAGGAAAACAAATAACTTTCAAAGGAGCAAGG  
CTGTGTTAAATTTAAGATATTTCAAGTTTGGGGCATTCTACTCTTTTCCACAACATAAA  
AACTTTTGAAAAAAGAACTTGAAAATTGTTTTCTTGTTACCACACACATTTTTTTTCA  
AATGCTTATATTTATTTATCCTTGCAATGAAATTTGTTTTTCTTTCTCCACAAAAAC  
CATTCTAGCTTTTTCTCCTTAAAACTTAACTTTTTGCCAAATTAGTCAAAAGCAATTTT  
TTTACAACAGTTTCAGGTTTTGTCCAAGATTTCAAAGACATTTTGAGGTAAAGGGTCATAAC  
ATAGTACAAATTTCTTTTGTCCGTATTATTTCACTCTATATAGTATTTTTGTAAAACCT  
AGTACTCTTTATACCAGAAATGGTATAAGGTACACCTTATACCAGAAATGCATTGTTGTC  
ATGCCTTCTTGCTGTAAC  
TGATACAGACAATCGAAGATGGAGACTTTAGCAGGAAATATATATGATTTTTTGGCCTATA  
ATCTTATTGAGTAGCTGTAAGTTATCTGTTATAGGTTAGTGATTAGAATTTATAGATGGA  
ATATTTCTAAGTATGGAGAAAATTTTTAATAGTCTTTAAGGATAGCATAACAAAACATT  
TTTTAAAGTTTAAAATAATACATGAAAAATTAACACTCATTAATTTTTAAAATTACCAA  
AATTCTGCCCATCGAGAACTGTTTCTTCTCTGGGTATTAAGGAGTCCAGAAAGGCAAGTT  
TCAGATAGTCCAGGAAGATTGGAGTTGAAGGCATATGATACTTTGATCAATACATAAATG  
AAAGTAGGAAGAAGTACTTGAAGACTATCATTTAGGAGTGATTTTTAAATGATACACATA  
ATAGAATATTAATACAACATTATTCAATTGTATTTAGAAAGAAAATGAAATAAAGAAGAT  
ATATATTTCAACTTCCATATTCTTATTTACAAGAAATACTGCATCTGCTATTTGTGGGAGG  
GAGAGACCCCTTCTCTGACCTGATTTGGCTTTTGATTTATTGATTGTGCTGTGGAGGTTCT  
GTTCAAGGCACTGAAGTTATTCTAAACCAATTATGGGGTCAGAAACCAATCTGTGGTCAAT  
TCCTGCAACTGAAGAGGACAGGAGTCAGACCATCCTCTACCAATAGCCTTGTTACCTTT  
GAATTTAATTATTTAAAAGACACTTTTCTGTTGTTTCTTTTCTGTCAGAGTATTTGGGAT  
GTTTGCCCACTACTGAAGACAGAGAGACTGTGTATGCCTGGTTTACCTTTTCACTGGCT  
TGATATTTGCCAATAGTGCTGCGAATCCAATTATTTATAAATTTCTCAGTGGTGAGTTTT  
AACTGTTCTTCCATAAGCCACAATTGTAACCAAGGATGAGGAATCAATGAACACTCTTCA  
ACTATATGAGGAGTTTAGTTGCTATGTGAGTTGTATTTTTTCCCTGACCTGATTTATCTT  
GAGTTTCTTCTCTTTTGAGGCAAAGTATTTGTTACTGAACTCATCAGAGAAAATGAACTG  
ATTTTTCCATGTCAAACGTATAAGAAATGTTATAATAGAAGAAAAGTAAACATTCTGAGA  
AATCAATAACACAAAATCTTACATGACATACTTTAAACTCATGATTTACAAAAATATAAA  
ATACTTTGTTCTGTTTTGCCTTGCTATATTATTCCTTTGCCAAAATGTGTAGCCTAATTG  
AGACAGAATTGGGATCTATTTCACTTTTAGATATTTTACTATATTTACGTTTCTCTGTGA  
GTATCATCTCTTGGATTTATCTCAATATTTCCCACTGACTACCAAAAATAGTATTACTCC  
AAAATAACACATAAGTTAAATGATACACACATACATATACGTGTAACCTTATACAATTTGT  
ATCTGTTTATGGAATCAATATAATTATAAAAGTCATTTAAATCACTATTGTTTATTCACA  
TTTTGCCCGACTGACTTTTGAATTTATTTTAAATTAGCTACCTTTTACATTGCCTTAAT  
CTCCAACCTCATTTGGCGATTTCTTTGTTATTTCTATCTTCAAATATATGGTGATTTTATGT  
GGAAGAATAGAAATTCATTTTGTGGCATATTTAATAAAGCTTCTGCATCTTCCAACCTGA  
TCTTTGGCCTTCTGGTTTGCATAGGTTTAAAAAAAAGGCAACAAATTAGATTGATGAGAA  
ATAATTTTGTCTATTTAAAAAAAATCTAGCACAAATGACTAAAGCTCTGAACCTCGCAC  
TAAGCAGGTAAAGGCTATGAGGAAGTTGTAATGAGAAGTGTTTGAAGCAGAAGTCACAGA  
ACCAGGTCAAAGTCCTAGTATGGAGGATAAAAGTGAGTTAGAGGAGGCAACTGATAATCA  
CTGATAACTCATTATGTGACTGCTATTGTGCTGGGCGCGTAACATTCTCTCTCATTT  
AATCACTGATAACTCAGTGCGTAGCTGAGGCTAAGAGAGAAGAAATGATTCGCAATACTG  
CCATTACACTAATAAAAGTGATTCATTCTCATAGTTCTCCAATATCTCCTCCATA  
ATTTAAAGACAAGGAATAGCTTCTACAGTATTTTTCCCCCTTCAGTTTTTGTCTTTCTT  
ATATAGATTATGAACTGAAAATTTTCTGGATATTTGAGTGTATGTTTCTAGGTATTTTG  
TGGATTTAATTGTTTCAGTATCAGTTATTTTAGAGTAAAATGCAGGAGTAATTTTGTATA  
ATTTTGGCTTTGTATGACATAAGTTTCATTGTGTTTAAATTATTAATATCTCTGAGAGTT  
CTTCTACTGATGATCACTTCCATTATAGTTATGTAGATAAAATATACCAATATGCGTAAA  
TATATGAGGTTTGACTATAAAGGAATGAAGCAAAATCCAAGCCCCATATGTGAAAGGCAG  
CCTCGTTATTTTATGAAAATATTCATTGTTTCAAGAGTCTACCAAGCTTCCAATAAACTC  
AATTTCTTATCTATTTTACCCATCTTTGCAAAATATTACACCTCATTGTTAGTTTGGC  
TCAAGGGAGCAACTCAGTTGTACCTATTCATAATTTGTTGAAGCATTTATGTATAATTC  
CTTTTCTTTCTATCTCTGTTTGGCAGGAAAATTTGAGAGGAATTTAAAGCTGCGTT  
TTCTTGCTGTTGCCTTGGAGTTCACCATCGCCAGGAGGATCGGCTCACCAGGGGACGAAC

FIG. 1AM

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TAGCACAGAGAGCCGGAAGTCCTTGACCACTCAAATCAGCAACTTTGATAACATATCAAA  
ACTTTCTGAGCAAGTTGTGCTCACTAGCATAAGCACACTCCCAGCAGCCAATGGAGCAGG  
ACCACTTCAAACTGGTAGAATATTTATTCATATGACAAGGATACCTGAGTAAAACTATC  
CTTTTTAAATCACTGGGAACAGAAATTTTATTATCCTATGATGTGAAGCTAAAAATTACT  
TGTGGATCTTTTTTTTTTTAATCTATTGCTCTTTGGAAATAAAAAAAGTCAGTTTAA  
AATGATTTCTCAACTTTTGATTTAAATATGTTAGAAGTTAACCTTCAATTGAGCTTATT  
TCAGGCTATTTCACTTTTAGTTTCATGTATTAAATGTGTGTCAATTAAATGTTTAAACA  
TTTCTAATTCTTTTTATAATCCCTTGTTATTTTAACTCTCTCACATTCAGATTGGTTCTTA  
AAAATTACCAGAATCTATCCAATGATTTTTTTTTGCTACTAAAAGAAGTAGCAATTACTAA  
TTCTGAATTAACAATAGACATGTTAGTTGACTTAATAGTTTTTTTTTAAAAAATCACAAG  
ACTGTTGTTATAATGTGATATCTGAGAAAATATTTATATATAAAATAGCATATTGTGTTA  
GGTAATTCAAAAAGTTTACAAAACCTATATACTCACTCATTTACACAATTTTCTCAGG  
TTTGCAAATTGACCATTGCTAACATTTCTTGCTCTCAACATATGGCCAGTAAGACTCTATC  
ACAGTAAAAGTTTTAACGTAATTTCCATCTCTAACACTTTAACATTTAAGAATAAGCTAA  
ATCACATCATTATATTCTTTTAAACAACAACAACAAAAGTGATATAGTCAGCCTTGCTGG  
ATTAATTTAAAAATGCACCACTGTGCTAGGTGCTAGGGAATGAGATGGCGTCGATGCAAA  
CATGCCCTTCAAAAGAGCTTCAGTCTAGTGAGGGAGACATGTTGACAGAGTGCAAGGCAGC  
AAACAATCTGGGGGACAATTCTTGGTCATGGCAGAGCAGTGAAGCTACCAAGGACAGTGG  
TCTTCAACCAGAAAGTTTGTAGCGCAGTTGCACTTTTTTTTTTTTCTTCAATTTAATTACAA  
TGACAGTTGATGTCAGTGGATTCCATCTGGGCCTGGGGCTGAGTACCAGGTGGTTAAAAA  
ATAGAGGGGCTTGCTCTTAACCTCACACATACATGAATAGACTATCGTATATTTTGTAGAA  
AATGTAAGATCTGGGAGTCAAAGCACTGAGTATTCAACTTATTCCCCTGAAAAATTCTT  
CTGATTCAAAATTTACTTGAAAAATTAACATAAAGTAAAAGAAGTGTTTATGAAAGATG  
ATTTTCATCTCTATTATGGTAACAGGTGTTCTGATTGTATTGAAACAAAAGATATGGGG  
CACAGTGTTTAAGAAAACTTTCATAGAAAATTAATTTTTGTTATTTTTTTCATTTTTTCCA  
TTACACTCAGAGAAAAGTAAAAGAGCCTAATTATCCACAACCTTGTTTTCAAATCTTGGAA  
TTTGGGATTCTGTTACCTTGTGCCTTTTATGACTCAAAGCAAAAACCTATCTTCTTATACA  
AGGTTTATTGAGATCATATTGTAAATATCAGCACTATATCAGTGAAAGCAAGGTATTTT  
AACTCTCTCCTTTCTCCCCCTTGTATATTTTAGAACCTTCTTTTCTTATTTATGCTGCATG  
AAAGGAGAGTTGTAATTTTCGGATCGTGATGACAGCACTTTAAAAAGTTTGAGGATAACT  
TCAAATAACGTTGATAATATGCCTTAATAGCCAGTAATAGCTCAGAGGAAGAGTAAATTC  
CTTAGACCCAAATATACCTACTTATAATTTAAAAGAGAGAAAAGGGAGAGAGATTGAGAG  
GGAAAGGGGGAGAGAAGGAAAAAAGTACTCAGAGAGCAGCAGTTATGTGACGTATGGGA  
AGTCAGAATTCCTTTGCTCTAAATCAGTGATTCTCAAAATGTGGTTTCTATACCATCGGC  
ATCAGCATCATCTGGGAACCTTAGTGGACATGCTAACCTCCACCCTATCCCTCACCTACTT  
AACCAGAACTTTAGGGGTGATAGCCCAAGCTGTGTGTTAAGCACTACAGGTGTTTCT  
GAAGCACTTTAAGATTTGAGATCCACTGCTTAAAGTGATACCATCTGACATCAGTTTATC  
TGCTGTGTGAAATAAAGTCTTTTACTGCACAGGTGTCTACAACAGGGGCCACCATCATC  
GCTACCGTCAACGTGGTTGGATGTCTGAAAGAAGAAGCTGAGTATCAATGTTGACTCTCA  
CTCATGTCTCTTATTAATAAAAAAAGAGTTTACAAAACAATTGCTACTGATAAATGCAG  
TGTGAAAGACTGGTTTTAAGGCACTTGTGTGCTTTATGTCCACCCAGATAACTTGAGTTT  
TTAACTAAAAGTTTCAAATCCCTATCTTCTTTTACTTACTAAAGTTCGTTTTGCAGAAG  
CAGATAGTTTCTAAGAATGATCATTTTCATGGAAGGAGATATAAAATAAAATAAAACCACT  
ACTTAAACTCTGGGAATGTAATAGGCCATGTACATAGCACTCAACATGTGAATCCAGGAA  
TCCTTCTAAGAGGTCTAGATTTAGTATGGTTACCTTAATAGGACAAATGGTAAAGAAATA  
GGTGTTCCTCAAACTCTGCCAATCTTATGAAACAAAGAGTCAACTCTTACCTCATTATTT  
GCTAATGACACAAATGCAAGACATCTTTTGAAAAGAATGTGTTGGGACTGTTTTATGCT  
GTACCTTGAATGTGTATCTCTCCTTTTTTTGCTATATTTCAAAGATTTAATGTAAGTTGT  
CAATGTCAATTGAGTTCTTGTATCAATAGGGATGATATAATTTTATCTAACATGGAATCC  
ATTTTAACTTTGTTATTTCTGAATTTCTATGAAACCACAAAAACCTTCATACTTGAATTT  
ATTTATTCTTGGCTAAAGATTACTCCAGTTTGTGAGGAAATTTATTTCTGAGTTTCCAA  
AGCTTGGAGAATTTATTGGATATTAATAACCTGTTATAAATATTGATGAGTTAATTGCA  
AGTAGCAGACACAATGATATTGAATTTCACTCCCAATACACATTTGTTTTAATGAAGATTA  
AGGTAATATGTTTTATAAAATTTAGTCTGGCTATGCTTAAACCTGAAATAGCAGAATGGC  
AAAAACCCCAAGCTGTTTATGGACCCAAATTTGTGAGGAGGGCTATTATTTTAACTACTT  
GTGTAATAATAGAATGCACCTTGATGTAAATTTGTAATAGCCATCAACTGCATTTCAAAAAC  
CTTTCGCTAGCCACTACAATTTAGAAAGCTTTTCAGTGTGAGTTAGTTTTACAACAAATG

FIG. 1AN

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CCTTTTCTACTTTCTACAAGTCACAAGTCAAAAAAAGTAAATTCCACCAAGTTTTATTTC  
AATTAGTTTTTCAAATTGCATGAAGCAAAAAATAGATTTTATAGAGACAATATATAAATAGA  
AAAAATATTGTAAAAGTCTACTCTATTACCTTATGTACCACAAAAAATAAAGTACAAAG  
GCATGAAAAACACTATTATTTCCCAAAGTCAAAGGGAATTGTTTTCTACGCAACTACTG  
CTACTAACAAGGGGACAACAACCCCTCCACTTGCCACGTATTTTTATTCTCTTTTCTTT  
ATATCTTTGGAGTTAAATGTCTTTTATGTTTTTCATGAAATGTATTCTATAATTGTTGTA  
TTTCATGTGTGTAACATTATGTCAGTTGTTTTAACAATTATCTTATATCTTGAAATTCTT  
TATGCCCTGATTGTACTGTGTCTTCATGAAGAAATTTCTTATCAAATCCAATGTGATTACA  
CACTTACTGCTGTAAAGGATGCGCATTATGTAGTTTTTAAGTAAAAACTATAGTGAGAAT  
TCTATAATCACATTCACACTCCCTCTCTATTGTATGAAAAATCTTGTTGTTGTTGATTGA  
GATAAGGTGGATATTCACTCATAGTTAATGTCAAATCTCTGCAGTTAAGGATTGAATTAA  
GCCCTCTGGTGCAGTACCTAATGATCAAAACATTTTTTCCAATAAGTTTATATAACCAAG  
GATAATAATGATATAAAAGGTTTTTAATGTTGTTTTTAAGAGCAGGTACTATAACAAGA  
AGTTTAAACACTGGTACAGAAATATTTTCATAAAAGTTATGAAAACCAGATAAATACAGTAT  
TAAATTTTGGAGCTTTTATCTGAGTTGAGAGATTTAGTCTACATTGACTGAGATGAAATG  
ATGAAGTCAATAATTTTCAATTTATTATCAGAATAATAAGTGACATTTACATAATTAATTT  
TTTTCTGGGCCATTTTGTATAAGTCATTTAGGACTATTTTAAAGTTCAGTGGTAAATTTTA  
AAATGTATATTTTCAAGCTTTTCAATTTTTTTCAAAATAGTTCTGAGAAATTACAGAATCA  
GATACTAAGGATATTAATTTAAAAATCAATTTTTATTTCAGCACTATTTATTCTAACATAT  
ATAAAAAATGAAGCCAAAGTAACCCGTCAAGGTAAATACTTGACTCCTAGGAAAATGTGA  
TTTTAGTAGGCATCTCAAGAGGAAGTGAACCTTCTCGTGGTGAAATTACAAGAAAAACAA  
GTTATTTCAGTGGTGAGAATGTGTTGCTCTAAGCAATCCATTAGCACAGACTAGCTACTTG  
GCCACTCCTCTTCTTCTGGAGCCAGCCCTGAAGAGTGGTCACAGCATCTTCATTTTTAT  
CCAGGCCAATGGCCATGCATGAGAAGTTGGGTAGCAAAATCTTGAAGCACCTCTTTGTT  
CTTGCTCTTCTTTCACTGTTTTCTCACTCTCCACCTGTAATGCTCACTGCCAGTTTTTACC  
ACCAAGCTAAGTATCAGCAGACCTCCCTCCACAGCGTGCCTTGCCCTGTAGAACCTCTGG  
TCCTTCCTTCAGCCCAACCCCATCCAATTGCCTAGGTTCTTGTTGTCTCCTGAGATGAAC  
AAGAGGCAAGTAGCTAATTTGAGAACAAATGAAGCAGAGCTGAAGGAAAAAGTAAACAT  
TTATTTTTTTCATATCCCAAATTTTATAATTTTACATTTTTTTTAAAACCCATTTCATTTTCT  
TCCCAGAACATTTATGCTTATCAGTGGTCTTCTGAATCTGTGACAACTCCCTTTTCAAGC  
CCCAGCTAAGCTTCTTGCCCTCAAGCCAGAAGGAATCCCAGTTTTTGAGTCTTGTGTTAAGG  
CCATGGCAGGTCAAGTGGGAGATTATCTGAGGAGGTACCGCTTGTGACACCTTCAGAAAC  
AAAACAGCTATTGCCTTACGTTTCATAGGCCCCAGGCCCTGAGCAATAGCAAAAAGATAAT  
ACTTATTTTTTTTAAACTGTTGTTTATTAGGTGATCGATTTCTAATTAATTTCAAATATTT  
TAAGGTAATATTTTAATTACCGAGGAAGAAATGGTACAAACAAAATGTTGTGGAACCTGGAA  
AATCCTCAGTGCTTGACAACATGAACTTATTTAACTTATTATAGATGAGATAATGAGAA  
CATCTTCAGAAAAGAAGCTATGTTCCTTAAACAGGGGTACAGATTTTAAAGCTCTGTTTT  
ATATGGTTTTTGGTAGACTAAGTGAAGAATTTGCCTATAAAGCTGAGTCTCGATCATATAG  
CATATCCATTATAAAGTGAGAAAATTGCAATTTTAGAGTATTGTCAATACATCCAAAAAT  
TTTTACATGATTTCTAAATGCAGATGTGTGTGTGTGTATGTCTACGTATGTCTCTCCATA  
TGCAACAAGCAGTTAATTAGTCCAAATATATCCACAGTGTAGATTAGTTTCATATCTCA  
GCTCTTCAATGTCTCTTCTTCATTTAATTCACCTCCTTGGTGTCTAGTTTTCTCCTCACTCTT  
TTACAAATATCCAGGTTCTATATTTCTGCTTTTTCTAGAGAGCTTTTTCCCTCAAGAATAT  
ATTTTTCTTTTTCTTTCTTTCTTTATTTTTGTTTGTTTTTAACTAACATTTCATATGGT  
TATAACAATTTGAGACAAGTGAAAAGGAAAGATCTGTAAACTGCCTATCTCCTTTGAAAT  
TCATTGCCAATAATCCTTAAGAATATAAAGTTCCTTGATGCCAAAGACCTTCTCATTAGT  
GTTGCTGCCTGTTGTTTCATTGGTTCCTTAGAACAAATGCCTGGCACATAAAAGTTATTTG  
ATAAATATCTCTGCTATTAATGAATTAATAAATACTGCATGACAATTCCTTCTCAATTC  
ATCATTTTTTGGTCATTTTCTCACAGTTGCTTCAATGTGTCTGTGGAACTATCTTTCCATG  
TGAACAAAACACTCTACATTCTCAGTGTCTACAAAGCACATATTTCTTTTTATTAAAAAT  
AAACTTTGAGAGCACCAATCCTAATGTCTAACCATCATCAAAGTGGCAGATAGCACCAG  
TATTCTTTTTTGTCTACCAATTTTATGCCAGGCATCTACTGTTTCTTTTCATGAATAAAAC  
CTGACACCTGTAAGAGGATTTATCATGGTAACTTCTCTTTGTTACTGACATTTTCAGCC  
TCTTGGGCTCTCCCTCCTTACTTATACACATTGGCAGCCAGCTTGAAGTCATACTCTCT  
AGACCTGGGTAAATGTGGTAATGCATCCAGGAATCCAGCTTAACTCTTCTTGGTCTC  
TTTGATGTGACTGACCTTTATTTCTACATTTCTTCATCAAACCAGTCTCACAGTTTGC  
CAGTGCAAATCACATGCTGCACCATGTGCTTATTATCTCCTATAACAACAGATGCTCCAC

FIG. 1AO



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TGAAATGCAAACTCTGTGTTAAGCCAACAACCTGCTTCTCCATCCTTTCTCCTATACGT  
TTCTTCTCACTACAACCTCCCTTCTCAACCCCAAGGGACTACTGGATTCTTTACTCTTT  
TATTTTACCCAGTCTATCAGTCCCATCCTGGACTTCCTTCCTTCTCTGCTTAGAGGAAA  
GCAAGATGATCAGGTAGAATTGCACCTATGACTAGATATTATTTACTTCAAACAAATTCT  
TACTATTTTGTCTGATGAAATTCATGACAGTTTTTCATACAACAGAAAGCCTGCCCTCTT  
AGAAGAGAAGAGAACTGAAAAGAAATGGTTGAAGTAAGGTAGAAAGCCCTCATGGAGTTA  
GGTGGCTAGGCCAGCAGAGCTAGGCACTGTTCTCCTGTTTCAAGATTGCACCTCTGATACT  
CCAGATGGGAAGCCTGCCATGGCACTAACCACAGCACTTTTATACCCTATCTCTGCTAT  
TATGAGCCCATATTAGTTTTTCTTCTGCTTCAGAAATTGTTGCAAAAAATAATTTTATTA  
TTTACAAATTATTTTTAAACCATATAAATCTGCTTAGTTTGATTCTCAAACCTCTAAA  
ACTTACACTTCTTGTGTCCAATCTTTGCTTTTAATTGGGTATAATTTGAGGCAGAAATA  
AATTAATCTCATTTTTTAAAAATGTACTAGCTATTAATAATTTTTTAAATTTATCTTCTAAA  
ATTGGAAAGTATCCACTTTAAATGCATCTGTAGCAAGGACTTTTTACATACATTCTGTAG  
CTTTATTACTTCCATTGAGAACTGTTAAATAACAGAACTTACCTCACTGTACGCTGGCT  
TTTGAAAAGGCAGCAGAACTGTTTATCTGATTATCGAAGTAATCATATTACATTTCTTTT  
TCTTTTCTAAGAGAAACCTTCTTCATGTGCTCAGTCAAACATTTTGGTGTTTAAGAATTG  
ACTTATTAGGTCAGGCGCGGTTGCTCACGCCTGTAATCCCAACACTTTGGAAGGCCGAGG  
CAGGTGGATCACTTAAGGTCAGGAGTTCGAGACCAGCCTGGTCAACATGGTGAAACCCCA  
CCCTACTAAAAATGCAAAAAAAAAAAAAATAGCAAGGTGTGGTGGTGCACATCTGTAATC  
CCAGCTACTTGAGAGGCTGAGGTGGGAGAATCATTTGAACTCGGGAGGCGGAGGTTGCAG  
TGAGCAGAGATCACACGACTGCACCTCCAGCCTGGGCGACAAACAAGAATCTGTCTCAAAA  
AAAACACAAAAACAAAAACAAACAAAAAAGAGTTGACTTAGTTAATGAAAATATTTTTT  
ATTAGGAAATTATACCTCTCTTTACAAAGTATGTATTATTTGTTGCATCTATATAGTCTA  
TCAATTCTAAAAGCACACTTTATGCGAAAATGTAGTCTAGGCCTTCAGAATGTATTATTA  
CAAGAAAGTATCTATCAACCATGTTTCATTTGTTTGCATGTTTTGTTTGTTCCTAATAG  
ACTATGAATATTCAGCTTCAAATGCTACCTCATGATTGTTACATTCCTGTTGTTGAAAGA  
ACCCATCTCTTTCTTACCTTCTTGTCCCTAAATGTGTTCTTCTTATAACTTACTTTGCA  
CATAACCATAATGGAGTGAGATCATAGAATTAAGAGGATTGAGAAAGAAAATACTTCCC  
TCATTCCATTGGCAGTAATCTGTGATTCAAAAGTTAACAACATACCATGTATTCTTGTAG  
GAGATTATTTTATGCTTATCACTGATCAACTTACATGCAGGTTAAACAGCCCTGAAAA  
AATGCTCATCATCACTGGCCATCAGAGAAATCAAAATCAAAACCACAATGAGATACCATC  
TCACACCAGAAGAATGGCGATCATTAAAAAGTCAGGAAATAACACTTGCTGGAGAGGATG  
TGGAGAAATATGAACACTTTTACACTTGTGCTCCCTAAATGTGTTCTTCTTATAACTTACTTTGCA  
GAAGACAGTGTGGCAATTACTCAAGGATCTAGACTAGAAATACCATTTGACCCAGCCATC  
CCATTACAGGGTATATACCCAAAAGATTATAAATCATGCTACTATAAAGGCACATGCACA  
CATATGTTTATTGCGGCACTATTACAAATAGCAAAAGACTTGGAACCAACCCAAATATCCA  
TCAATGATAGACTGGATTAAGAAAATGTGGCAGATATACACCATGGAATACTATGCAGCC  
ATCTGAGCAAACTATCGCAAGGACAGAAAACCAACTCCGCATGTTCTCACTCATAGGTG  
GGAATTGAACAATGAGAACAATTGGACACAGGGTGGGAAACATCACACACCGGGGCCAT  
CATGGGGTGGGGTAGGAGGGAGGGATAGCATTAGGAGAAATACCTAATGTAAATGATGA  
GTTAATGGGTGCAGTACTCCAACATGGCACATGTATACATATGTAACAAACCTGCACGTT  
GTGCACGTGTACCCTAGAACTTAAATATAATTTAAAAAAGCCCTAAATGCAACTT  
GTTCAAGATAACTGGAGCCATCTTCTAGCTCTTTATTTCTCAGACAGTGTGGGTAAGTCC  
TGCTCCGTACGAATGCTTATGTGAGTTTGAAGTTCAGTACTTTCTTAAGAGCCAGAGTC  
AGTCAAGATGTTCCCTTAACAAGATTTTTCAATGGGGTTACACATTAATGAGTTCTTTTT  
CCTCCTTTAAGTATTTGAAAATTTTGGTTTAATAAAAGGTTTAACTATGATGAATTTAGG  
ATCCTTTTTCTGTTACAGAGCACAGAATAATAGTTAATATTTTACATACATATTGCAAG  
TTCATGTTGCCACTAGGAGTGTCCAGAATAGACAATTGAAACAGCCTTCTAGCTACTACT  
ATCAAAAAAGAGCTTTAAATAACATATTTTAATTAATAACATTATTTTCTATAGCTATA  
CCTCAATAAAACCATCAACCAATGTTTGTACAATTTGATGCCCCCACTCTAAGATTTTTTA  
GCTAGTGTAATCAGAGTCTCCTATTTAATGAGACACTTTATCCAATCAGGTTGTGTTTA  
TTATTCAACCAGATGATCTTGGAACCTATAACAACTAGTAATACTTAAAGCTGGGCTTT  
ATGTGCGTGATTTACTGGGATGTTTGCTTATACCTTGTTTCCAAGCTAAAAATATTGTGA  
CCAGGTGTGTTAGTCTGTTTTGAGTTGCTATATAGGACTACCTAATGCTGGGTCAATTTAT  
AAAGAAAGAGGTTTATTTGGATTATGGTCTGCAGGCTGTACAAAGAGCATGACATCAG  
ATCTGCTTCTGGTAATGCCCTCAGGAAGCTTTTACTCATGCCAGAAAGGCAAGGGAGCC  
AGCGTGCCACATGGCAAGAGAGGGAGGAAGCACAAAGAGAGAGGAGACGTACCAGGCACTT

FIG. 1AP



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TTTAACAACCAGCTCTCACATGAACTAACAGAGTGATAACTCACTCAATACCCGGGGGAT  
GGCACCAAGCCATTCATGAAGGATTTGCCCTCATGACCAAATACCTCCCCTAGGCCCCAA  
CCTCCAACACTGGGGGTCTCATTTCACATGAGATTTGGAAGGGACGACTATCCAAACTA  
TATCATCAGGATTTTCTGGCATGGACTACCAAGCCATTTCTGCTTCAAACCTCCCCTGAAA  
TTCTTGTAAATGCAGATTCTTTGATACACCCCAATACACTATTTAGTCTGAGATG  
AAACTCAAGGATTCTGATTTAATTGATCTAGACTAGCATTTGACCATTGATTTATCATCT  
GGGATTCTAGGAAGTCAACCCTTATATGTTTTAGAGCAGACTTCATTATAATTGAGGAG  
AATGTTTGTAGTCTGTGGGCTCCTCTGTCCACTTCTGATTGGGGCCCCCTTTGCCTGATTC  
TGACTGGATCAGGCAGAGTTTTATTCAAGCCACTGTCTTTTGGCTTCTTAATGTTCAA  
AATATATTAACACAATCTCAGTTTTCTAAGAGCTAAATTATACGACTTGGTTCTTGTCTG  
GTAACATAACTGCATTACTGGATCTTGTCAAGATTCAGAGACATTTCTCCAGTTTTCAAAT  
TTGTAACATAACACTGTTTGTATCACAAAAAGTTCTAAGCCAAAGCAAACTCTTTCTACC  
ACCACCAGATGGCGTTACTTTGGACTTACCTATAAATGGATTTCCAAATGGTTTTTTCAGA  
AACCAACTGGAGGTACTTAGAAAACTTATGGAACCTACAACATTTCTTTGCATGTCAAA  
AGCTATAACAGTAAATAATATTTGTGGAGAATATCTGTAAAGATTAGGCTGCCTTTCTTT  
TCCTCCAGCTTATTTAACTATATCCTTATATTAACCCCTGTTGGAGATGTGTCTCTTA  
TTGCACTGTATGTGAGTGTGTGTGTGTGTATCCCATCACGTTGGTATGATGATAGCACCC  
TTCATTGAGAAGCTTTGCAAAAAGAATATAAGAACATGTTATTATGTTTACTTAAAGTA  
TAAGGCCGGGTGTGGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCAAGGTGGGA  
GGATGACGAGGTGAGGAGTTAGAGACCAGCCTGACCAACACGGTAAACCCCTGTCTCTAA  
TAAAAAATACAAAAATTAGCCAGGTATGATGGCAGCATCTGTAATCCTAGCTACTCAGG  
AGGCTGAGGCGGGAGAGTCCCTTGAACCCAGGAGACGGAGTTTGCAGTGAGCCTAGGTGG  
CGCCACTGCACTCAGGCCTGGGTGACAGAGTGAGACTCCATCTCAAAAAAAGAAAAAAG  
AAAAAAAGTATTGAGGACATTGCTCATGACATTCCAAGGTTATATAAAGAATATATAA  
AAAGAAATTTCTGCCTGGACTTAGTGCCAGGAATACTTGTACTTTTCTTGCTTTCTTCTT  
AAGAACATTGCACAATAGAGTATTTTAAAAATTGTGCTTGCTGTTCAAATTGCCTGCTG  
GAAGGATTAGAGGCAGATCTGTAGCATGCCGAGTCCCATCTTTCATACAGGCTCATG  
ACAAACATTGTATGTGCTAATTCTATCTGGCTTCTCTTTATATTCTATCTGTCTCTATT  
TCCTGTCTATTTTAAATGTTTTAAATTTGTACTTTTACTTAAATGGTTTTTGGGAAGAAATA  
AATATAAGTAAAGTCTGTTAGAGGCCCGGCGCGGTGGCTCACGCCTGTAATCCCAGCACT  
TTGGGAGGCCAAGGCGGGTGGATCACAAGGTCAGGAGATTGAGACCACCCTGGCTAACAC  
GGTGAACCCCTCTCTACTAAAAATACAAAAAATAAATAGCCAGGCGAGGTGG  
CGGGTGCCTGTAGTCCAGCTACTCGAGAGGCTGAGGTGGGAGAATGGCATGAACCCAGG  
AGGTGGAGCTCGCAGTGAGCCGAGATCTCACCCTGCACTCCAGCCTGGGCGACAGAGCG  
AGACTCCGTCTCAAAAAATAAAAAATAAAAAATAAAGTCCGTTACAAAGCACAA  
AAAAGAACGGCAAGCCAACAAACATATGAAAAAAGCTCATCATCACTGGTCATTAGAG  
AAATGCAAATCAAAACCACAATGAGCCATCATCTCACGCCAGTTGGAATGGTGATCATTA  
AAAAGTCAGAAAACAACAGATGCTGGAGAGGATGTGGAGAAATAGGAACGCTTTTACAC  
TGTTGGTGGAGGTGTCAATTAGTTCAACCATTTGTGGAAAGCAGTGTGGCGATTCTCAAG  
GATCTAGAACCAGAAATACCATTTGACCCAGCAGTCCCATTTACTGGGTACATACCCAAAG  
GATTATAAATCATTTCTACTATAAAGACACATGCACATGTATGTTTTTGCAGCAGTACTC  
ACAATAGCAAAGACTTTGGAACCAATCCAAATGCCATCAGTGATAGACTGGATAAAGAAA  
ATGTGGCACATATAATATACAGCATAGAACACTATGCAGCCATAAACAAGGATGAATTC  
ATGTCCTTGGCAGGGACATGGATGAAGCTGGAAACCATCATTCTCAGTAAACTAACACAG  
GAACAGAAAACCAACACCACATGTTCTCACTCATAAGTGGCAGTTGAACAATGAGAACA  
CATGGACACAGGGAGGGGAACATTACACATCGGGGCCCTATTGGGGAATGGGGGCTAGGGG  
AGGGATAGCATTAGGAGAAATACTTAATGTAGATGACGGGTTGATGGGTGCAGCAACCA  
CCATGGCATGTGTATACCTATGTAACAAACCTGCATGTTCTGCTCATGTATCCCAGAACT  
TAAAGTATAATAAATAAAAAAAGAAAGCACAAAAATAAAGTACTTGGAAAAGTTTAA  
GGTTAAATATTATGCAAACTGAAAACCTAGCTTCAGATACATTTAAGTTTATATCATGT  
TAACAAGTTATTTCTTTCTAAAAAATTCTAACCTGTAACACAGAGAGTGGACTTGAACCT  
GAAAATATGGTTAAGGTACAAATGCAGATTTGGGGTCCCAGTCTCCCAGACTGTGGCTTC  
TATGGAAGAGATTGTACTGGCTCCAAATTCACAGATGATTGAACAACCTGTTTCTGCCT  
GTGTGAGAGCTGAAGAGTGAATATCTCCACTATATATATCTCAAAATCTCCCAATGAAA  
TTTGGTAACCTCTATGCCATAACACATCACATTAATAATTTGTATTCAAAGTCTCTCA  
GAAAAGATTTTGAATGCCAGATACCTTAATTTTTTATGTTTATATATTTAGGGTGT  
TGAGTACAGATTTCTTACATGCCTATATTGCATAGTGGTGGAGTCTGGGCTTTTACTGTA

FIG. 1AQ

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GTCATCATCTGAACAGTGAACCTTGTACCAAATAAGTAATTTTTCAACTCTCATCCACCCA  
CCCTCCCACCTTTTGTAGTACCCAAGGTCTATTATCCCACCTCTGTATGCCTGTGTACCTA  
TTGTTTAGCTTCCACTTATAAGTGAACACATGCAGCATTTGACTTTCTGTTTCTGAGTTA  
TTTTACTTAGGATAATGGCCTCCAGTTCATCTACATGGCTGCAAAAGTTATGATTTTAT  
TCTTTTTTATGGCTCCATTATATGTATGTGTGTATCTCAATTTTCTTTATCAAACCT  
CTGTTGATGGACACTTAGATTAGTCCACATTTTTGCTATTGTGATAAACATGTAAGTGCA  
GGTATCTTTGTAATATAATGATTTCTTTCCCTTTGGATATATACCAGGTAGTGGGATTTC  
TGGATCTAATGGTAGTTCTATTTTTAGTTCTTTGAGAAATCTCCATACTGTCTTCCATAA  
AGTTGTACTAGTTTACATTTCCACCAAAAGTGTATAAGCATTCCTTTTCTCTGCATCC  
TCACAAACATCCTTTGCTTATTGACTTTTTAATAACAGCCATTCTGACTAGTGTGAAATA  
ATATTTTATTGTGATTTTAAATTTTCTCTGATGATTAGTGATGTTGAGCATTGTCTCAACA  
TCACTATGCTAGTGGCATGCATGTTTTCTTTTGAAAAAAGTTTGTGTTCTTTGCCACA  
TTTTAATGGGGTTATTTGTTTTTTTTTCTTTGAGTTGTTGAGTTCCTTGTAGATTCT  
GAAAATTATTCCTTTGTGAGCTGCATAGTTTACAATTTTTTCCATTCTGTAGTTTGTCT  
TGTTCACTCTGTTGATTGTTTATTTTTCTGTCCAGAACTTTAGTTTAAAGTCCCATTGT  
CTATTTTTGTTTTTGTGTCATTTGCCTTTGAGGACTAGGTCATAATTTTTTGCCTGGGCA  
AATGTCCTGAAGATTTTTTCCAGGCTTTCTTATAGTATTTTTATAGTTTCGGGTCTTAT  
GTTTAGGTCTTTAATCTATCTTGAGTTAATTTTTGTAGCTGGTCAGAGGTAGGTGTCCAG  
TTCAATCTTCTACATATGGCTATCCAGTTTTCCAGCACCATTATTTGAATAGGGAGTC  
ATTTACCCAGTAAATATTTTAGTTGACTTTGTTAAAAATCAGTTGGTTATAGGTGTGTC  
TTTTATTTCTAGGTTCTCTATGCTGTTCTATTTCATCAATGTGTACATTTTTATACTAGTA  
CCATGTTGTTTTGGTTACTATAGCTTTGTAGCATAATTTGAAGTCATAATATGATGCCAA  
CAACTCTGTTCTTTTTGTTTGAATTTGCTTTGGCTTTTTTTCCTTGTGAGAGTTTGTCTGA  
GAATGATGGTTTCCAGCTTTGTCCATGTGCTACAAAGGACATAATCTCACCTTTTTTTA  
TGGCTGCGTAGTATTCATGGTGTATATGTGCCACATTTCTTAATCCAGTCTATCATTG  
ATGGGGGAGGGGGAAGGGATAGCATTAGGAGATATACCTAATGTAAATGACGAGTTAAT  
GGGTGCAGCACACCAACATGGCACATGTATACATATGTAGCAAACCTGCACATTGTGCAC  
ATGTACCCTAGAACTTAAAGTATAATAAAAAATAAATAAATAAATAAATAAATAAATTGCTT  
TGGCTTTCTGGACTCTTTTTTTTTGGTTTTATATGAATTTTAGGATTTTTTTCTAATTCTA  
TGAAAAATGGCATTGGTAATTTGATAGGGATTGTGTGCAATCAGTAGACTGCTTTAGACA  
GCATGGTCATTTAATAATATTGAATCTCTAATCCATGAGCCAGGGATATTTTTCCATTT  
GTTTTTGTCTAGGTTTTTCTTCCATCAGTGTTTTGTAGTTCTCCTTATAGATATCTT  
TTACCTCTTGGTGAAATGTATTCCCAGGCATTTTACTTTATCTTATCTTTTTGTAGCTA  
TTATAAATGGAATTGCTTTCTTAGTTTGGTCTTGGAAATGCCAACTACATTTAAATCC  
TTTTCCATTTGATGGATTTTCAGGTCTTGATGAACATCTCAGTTGTAATTTTCTTAAGATT  
GAAAAAGTAAATATTTTTTCTATATGTATATATAAAATGTCCCTCTCTCAAAATTTTAAAT  
TCAATAACCTGCTAGATATCACTTTAGAATCTTGCACTACTAGTTTCTTCTCAATTAAT  
TGATAGTATCTTTTAAATTTGGGCATGTTTTTCCCTATTAGGACTTAAGTTATTAGG  
ACCTAAGTTTGTAGACAAGAACTATGTTATATTTGAGAAATTTGTGAGTCATGTACTGGG  
CCTAGCACAGTGCCTCATAAGATGTAGACCCTCAATAAACTTGTGTAATAGGTTAATAAA  
TAAAAAAGCCCTATCACTCAATTTTTTTTTTTTTTTTTTTTAGATGGAGTCTCACTCAGT  
CACCCAGCCTGGAGTGCAGTGGCACGATATCGGCTCACTGCAAGCTCTGCCTCCTGGGTT  
CACACCCTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGACTACAGACACCCGCCACCATG  
CCCGACTAATTTTTTTGTATTTTTTAGTAGAGACGGGGTTTTACCTGTGTTAGCCAGGATGG  
TCTCGATCTCCTCACCTCATGATCTGACCCCTCGGCCCTCCCAAAGTGCTGGGATTACAG  
GCATGAGCCACCACACCTGGCCTATTTTCAGTCAATTGTTAAAAGTGCTAAGAACAAGTGG  
AGATCTTGTTAATGAAGAAAAAATAAGTATTTACTACTTACCTAAACACTCTACTAA  
GAAGGGATATACAGATCAAAAGGATTAAATCTCTGCCTGCATTAAAGCTAACTGTTTTGTA  
AAGAAGAACGTAAACAAAGTCAAAATGCATTTTTTAGGTGCTAGAGATTAGACAGGACA  
AAATCTTCTGGCTCTGCCTAGAGTTAAGTGGCTTTGGGAGAGGCTTTGCTGTAGTTTAAA  
GGCAGAGGTGGGGAAGGCCACTCTGGCCACAAGGACAGATCCACAATGGGATGGGGTATG  
AAACAGCACGAACCTTTCAGGAAATTACACATAATTTAAAAGGAAAATGGGAGCCCATGG  
CAGAAAATAGAATTGAACAGCAGGAAAAGGGTAGATAGTAAAAAGCATTTTATAATATTC  
AAGGACATTTGAAACTTGTGGTATACAATGAGGAAGAATTTAAAAATCTATACAGAGGA  
GTGACATAGTTAGATTTGTGTTCTGGGAGCATATAATAGCATTACAGCGGGTGAATTT  
GAAAGCTGGGCCTCAAAAGTTTAGATCTCAAAATAGGTTTTTATGGGAGTATTCATCTCA  
TGAAACATGATTTGGAATAAACAAGGCAGTGGCAATGGGGCTGGAAAATAAACAAGTAG

FIG. 1AR

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ATTTTCATATCTAGATGAAGATTTGTGGAATAAGAGAGGCCACATTAATGTTTAATTCTAT  
TTACAATGGATCCCAGCCACCATCCGCTTTAACACAGAGGTGCTTTTCCAGTAGCTAAGA  
GGACTAGGTGCTTTAGATACATTTGTGAAGTTGCTCTCCATTGTTAACATGCTTTTTTT  
ATTGCTCTGTGTGTAGGTTGATGGGGGAGGCAGAGTTAGGATCACACATAGAAGTTCAGTC  
TTTGAAATGCTTTCTTTCTCTTTTTTCCCCAAACAATGACCCCCACCTTTTCTTCTGGCA  
TATGTTGCCCTCAAGACCTAACACTGCTGCCAATCTGCTGGTCTTAGAGCCAAGAATCTG  
CCACCACCTGGCCCACCACAGCCTGCTCTGCTAGCTGCTCTCCTGCCAATACTGGCCTTC  
ATGTACAAGTGTAGGTTTTGAGGGTTCCGTTCTCTCCCCCTTTCTCTCTTTGAGTGTGGG  
TTTGTGAGTGTGTGTGTCTTCTGTAATAAGAAGAAAACAGGCCACATTTTCTCTACTCGT  
GTTATACACTTCCCGGAGTGTCTCACATCAAAACCTGTCTAAGTCCAAGCCTTAGAAGC  
TCTTTGCTGGCCCAGCCTACACTTGGGTTGTTACTTCTCAGGAGCTACCTTTCTGTCACT  
TGAGATTTTAAACAACCCACCACAGTACTCCAAGCGTGCAGTCCCTCACATCTTGAAATCT  
GTGCTTTTGGCAGCAGCAGAATCAGGGGTCTGTGGATTCTGAACCCAGAATGTGTCAAACC  
AAAGGGTGACATATTGGGACATTTAATAAGTCAGAGACTATTTCCCAGGAATATTTTTTT  
GAAGCATTTAACTAAAATACAATTGAACTGAGATCTCAAAACAGGAAAAATGAACTTGA  
CAAGAATTAGGCTAAGCTGCATCTCATGACGTAAATATTCACATTTGCATATACATTAAC  
AGAGTCAAGTCAAAAAATGATTTTTTATTGGATAGGATTAACCTTAGCTACAGAAAACAG  
AAAGTTTAAATGACTGGCTTTAAAAAGCAAAAGTTTACTTGCTTTCATTTATATGCAATC  
TGGGGGGTTGCGGGGGAAGATTTGTTTGTGGGTTTCCCATTCTCAAGGTGCCAGGCTCCT  
GTGTTTCTGCCCCATATCCTTAGAGGGAGGGTTTCTCCTCAGGATTGCCTTATGTGCAA  
GGTGACTACTGAAGCTCCATTTTTTATGCCCAAATGTAGCAAGAAAGAGAAAAGGAAGA  
AGGAACAGAAAGGCACATGACATCACTTCAAAATAAAATTAGGGGGAAAATAATAACAGAT  
ATCTGATAGGAACTAACAGTACCTTCTGCAATAATGATTACATTTCTGGAAAATAAATG  
TTAAGATCCTTGAAAACAAGGAGTAATAGTTGAGGAAAAGCTTCTTAGCAGCCTGGGACT  
AAAAACTTCAAAAAATTTAAGATAAAAAATCTGAAAACCTGGTAGAGAATTGGGGAGAAAA  
GAGAATTTGAACAAGGCATGCAAGAGTAAGAAAAATGTCATCACAAAATTACTAAGAAAG  
CATAAAAGCAACTATATTTTATTAGAGTAAAAATAAATGGATTGAATAACCTAGTAAAA  
TAAATTCAGCCATACATTGTTTATAAAAAAGTGATTTAAGGTGATTAGGAAAAAATAAA  
ACTAATTTAAGTGCAAAGATCTCCCAGGGAAGTCAAAGCAAAAATAAAGTCAGATGTTG  
CTGTCAATTAGACAAAGTAAATTTAAGGTGAAAACATGACAAAGAGGGACATTAATAAG  
GATAAATGTACAATCAATGGTGACAAACTTTTATAAACTGAAATTATATTAACAAAAACA  
TAAATCATGTAAACTAAAATACCTTGATAAAATGCAAATTATCAGGTAACAAGAATATA  
TCTATTGCAGAAAGTAATATATCAAACTAAAATAATGTGTATCTATTACAAGTATACAAT  
ACTTTGTAGCCTACAAAATAAGAATATACGATTTCTTCTTAAATGTTATACATTTACAA  
TAATTAATAATTTGGCCACTCAGAAAACCTTGGTAAAGCAAGGAAAGTAGAGATATTATA  
AGCCAACCTTAATAATTTAGTAACATTGGGTAAAAATGGAAGAAGTATCATATTGTGGTTG  
TGAACATAAGCTCTAGTTCTCCTAGTTTTGTGATTTGGGAAAGTTAATTATCTTCTCT  
ACCTCGTCTTAATTTTCAGTAATATTAGGATAACAATAGTTTGTACATCATCAGTGTTTT  
TTTTTTTTTGGGAATAAATGACTCACATGTATTAAACACTTAGATCCATTGTTAACATAT  
AATATGTATAAATAATGTCAGTATAAATCAATGTCAGCCTAAAAAGTTAAGACTGTGATT  
TTAAATAATACTAGATTTAGAATAAAATCAAAATTGAAATGACATTATTAACCTAAAAAT  
AACAAAAAAGAGAAGACTTTAAACACAATGGATGGAAGCAGCTATACCAATAAAAGAC  
AAAAATGTGGAGTATTATATGTTCTTAATGTTTTTTAAATTTAAAAATAAATAAACTA  
AAACATAGAATTTTAAAAATTAAATGTTGGAGGGATTAGGTCAGATAAGAGAAATTTCTG  
TTAGCAGCAGCTGAATTTTCTGCTAATAACAGAGAATTGTGAAAAGATGATTTTCATAAAT  
ATGGCAAATGTTTGTAAATAGCCATCCTAGGAGCACGGATATTAGTAACCTAATTGAGGAAG  
TACTGTTGGGCAGTGTCAATATACTGGTTAAGAATAGAATTTAAATAATGCTAATTATA  
AGGCCAAAAAAGTCAAGTAAATGCAATTTTTTTTGTAGTATAATTCAAGTAGGGGAGAAGGAGAGA  
TAATTAACCTTGAAATTGACATACAGTTGTCCCTTGGCATCCATGAGGAATTAGTTCCA  
GGACTCCCTATGGATACCTAAATTCACAAATGCTCAGGTCCCTTATATAAAATGGCAAAA  
TATTTGCATATAACTTACACACACCCTCTTTATAATTTAAGTCATTTCTAAAGTACTTAT  
AATACCGAATGCATTATAAATGACTGTGGAAATAGTTGTTGTATTATTTAGGGAATAATG  
ACAATAAAAAATATATGTATATGTTTCAAGTAAACAGATGCCTTTTTTAAAAAAAATGTTTT  
TTGATCCACAGTTGGCTGAATCTATGGATACAGAGCCACATTTACTGAGGGCAGACTAT  
ATTTAGAGTACTTAAGGATCACAGGGACACACATCTGAGGGTACTGAAGAGTGGGAAGA  
AATTACTAACCAGAGGGTCAGACTAGAAGGCAAGGAAGTGAAGCCAGGAGATGATTAGAA  
AATAAGAAAATCATACAAGCCTGGAGATTATGTTGAAGTGAAGAACATAATTAGAGTGA

FIG. 1AS

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GAAACATGAGTCAAGGAAGAAGGAGATTGGTGCTTGAGAGATGTGGCAGACTGTATCTTT  
CAAAGATGGCTACACCAATATATATCTCATTCCACAAGCTGTTTTTACCATGCTGTATTG  
ACGCTCTTCCATATGGAGGTGGGGCCTATGTCCCCTCCCTTGAAACCAAATGAAACTTTG  
TAATTGCCTTGATCAACAGATTGCAGTAGGAGTGTATGCTGGATGATTTCAAAGGCTAATA  
CACACAAGAAAATAATGGCTTTTCATTTGACTCTTTCTTGGAACATGTGCCTTGGAAACCA  
TGAGCTTATTTGCAAGAAGCTCAGCTATCCTAAAGTTTATCTACTGGGTAGACCAAGTGG  
AGAAATTACACAGACATTGAGATTATGTTCAAGGGGTCTCAGAGGTTCAAGGCCTCCCAA  
TTCAGGCACCAAACAAGTGGAGAAAAGGCTTTTCAAGATCATCCCTCTGAAATAATTGTCT  
GATTGAAACCTCAAAGAGTCCCTGAGCCAGAACCATCCAGCCAAGCCACTCTCAAATTC  
CAAATCCACAGACACCATGAATGACAGTAAATCATTATTGTTGTTTTAAAGCACATAAGT  
TTTGGGGGGTTATTTACACACAGCAACAGAAAAAAAAGTGAATGGGAAACATGGAG  
AGAAATGCAAATAGAATAAAATGGGAAGGAATACAAGGAGAGGAAAGTAGTATTGTGCAA  
AATAGGCAATCGGATGACCCTCAAAGGAAATTTTTTTTTCTGAGCAACTTAATGAATATA  
AGGTCAGATTAAATTGGAAGGTAACAGGTACAAATATCATTAATGCTAAATTCTATTGT  
AGTAAGTCAACTATTTGTAAATTATGCATTGGAGACCGACTTTACATCAATCAAAGTTA  
AATTTATTTAGAAATCTATAGAAGAAGAAAAAGAATAAAAGCCATTGGAAAAGTTTTTAC  
AATTATTCATTAAATAGACAAAGTCCTTTAAAGGAAAGGGATTAAATGAAGGTAAGGTG  
ATCTGCTTAAAAATAATATAGCAATCTGGGAGCCATGGCTCATGCCTGCAATCCCAGTGC  
TTTGGGAAATCTAGGCAGGAGGACCTCCCAAAGGAGGACTTGGAGTTTGAGACCAGCCTA  
GGCAACACAGAGAGACTCCATCTCAAAATTTTAAATTTCTTAAAGAAAAAAAATAAAAT  
GAAATAATATTGTATTAAATCCAGTAAAGCATCAGACCAATTTAGAATATGGATGAGAG  
AGAAAAACTAGAAATAACACCACAACAAGGAAGGAGAAAGCTGGTCTCTGGCAGGGACTT  
CTAATTTAGAGAAAGACAGATGATAGCAACAGCAAAAGTTGTATTATAGATGTAACCTA  
AAAATAATTTGATTTTTATTTTTAGTCAGAAAAGTCTTTAGGTATGGAACAAGTATAA  
CCTGGTATTTCCAGTATCTCTCTGTGACCTCACATCTCTCTCCAGATACTGCCTCAATT  
CTCTGCTTCTCTTTATAGCAAATTCCTTGAAAGAGAGACTACCTGGATCAGAAATTCCT  
CTGCTTCAATTTGATCCTGAATCCACTTCATCTAGATCTTCCTCACCATTCCCCCAAT  
ATTTGTCTTATTATGGTCACATGGGACCTCTACTTTGCTATATCAGTAATTTTGTCTCA  
TTTTACTTTTTTGTAGTTAATTACTCCCTTCTCCTTGAAACACTTTCCTTGTGTTGGCTTC  
TAGGATGCCCTGTCTCATGGATTTCCCTTTCACTTCTCCAGTCATTTCTGTTTGTTTTTT  
CAATATCTTCGTGATCTTATATTTTTAATGCGTCCGTGCTAGCTTCCCAACTAGGTTTCT  
ACTTTCACCTTAATTCCTATGGTTTATTTCTCTACAAGAAAGGAATTATAATCCCTTAAA  
AATGTCAATAAAACTCTATCACTACTCAATACTCTCCAAGGGGTCTTATTTTATTCAAG  
TAAAAAACTAAAGTCTTACTATATGTCTGTAAATTCCCATAGGATCTGGCCCCACAGCC  
CCTCTGGCCCCCTGTCCATTCTGCCCCCTTGCCAATTCGCCCCGGCCACAGTTGCCCAATAG  
CTGGTCTGTGAACACATCAAGCACATACTTAATCTCAAGGCTTTTGCAATCATTCTTTTT  
TCTAGTTGTAATCTCTCATTAATTTCTGAGTGTCTTGTCTGCAAGTTGCTTTACTTA  
CTTGACCTATATAAAATAGTAATTTCTTACCCCTACAACCTCATTATGTCCTATCTTCTT  
GCCTTGCTTATGTTTTTTTCTTGAGTTACAGATACCTGATGTAGATAGTATTTACTTT  
TTTTATGCTTGCATTAATCACCTAGAAATATAAACTCCAAAAGAGGAGCTATTTCTCTTT  
ATAATCTATCTAATATATCTTGATATTTGCTCCCACTAAATTTTCATGTTGAAATGTAA  
TTCCCTGTGTTGGAGATGGGGTCTGGTGGGAGGTATGTGGATCATGGGGCGGATCCCTCA  
TGAAGGGCTTGGGCCATCCTTTTGGAGAGAAGTGGGCTCTGGCTCTGACTTCACACGAGA  
TCTGGTTGTTTAAAAGTGTGCGACAGCTCCCTGAGCTTCCTCTCTCACTTGCTCCTGCT  
TTTGCCATGTGAAGTACCAGCTACTGCTTCATTTTCCACCATGAGTAAAAGATCCCTGAG  
GCCCTCCCTCAGCAGTACATGTCCCTATGCTTGTGTGCGAGCTGGCAGAACCATGAGCCA  
ATTAAATCTCTTTTCTTTTAAATTACTCAGTCTCATGTATTTCTTTATAGCAATACAAGG  
TTGGCTTAATACATATCTCTAAAGCAAAAGCTGGGCCTGGTATGTAATAGGTGTTCAATA  
AATATTTATTGAATAAATGAATAAAATACTAGGCTAAATAAAGTTTAAAACATCATAATAG  
AACACTGGGTAGATGTCAAGATGACAGTTTTGTTATTACATATGGACATGGAAAGGTCT  
TTGTGGTGCATTGTTAAGGGAGCAAACCAAATTACAGAACACTATATAGAGTAGAGCTGT  
ATAAAATACATATGGTGTATGTTTATAAATATGTCTAGAAAAATTTGAAAGCTATATATC  
AAATATCATATCATTTATCTTTAGAAGGCTAATTGCATATTTTCAATTTATTGTTTATAA  
TTTTTTTTATCTATTATTATAGGTTACTTGATAATCACAAAAGACAACCTGAATAATTCT  
TTTTGTCTTCATCAACTTTTTATTTAAGTTCTGGGATACATGTACAGGATGTGCAGGTTT  
GTTACATAGGTAAACGAGTGGCATGGTGGTTTGTGTCACAGATCGACCCATCACCAGGT  
ATTAAGCTCAGCATCCATTAGTTATTCCTCCTGATGCTCTCCTTCCCTTGGCCACCAA

FIG. 1AT

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TACACCCTAGTGTATGTTGTTACCCCTCATGTGACCATGTGTTCTCATCATTACAGCTCCC  
CCATATAAGTAAGAATATGCAGTGTAGGTTTTCTGTTCCCTGTGTTAGTTTGCTGAGGAT  
AACAGGTTCTAGATCCATCCATGTCCCTGCAAAGGACATGCTCTTGTTCCTTTTTATGGG  
TGCATAGTATTCCTTGGTGTATATGTACCACATGTACAACATAATTTCCACAACAAAAAT  
GTACTATTACATGGATATAATGTTTATATTCTCTTACAGAATTTGAGTCACTTGAATTT  
TTGCTTTAACACTTAGAATTTGGAGGGTCTGTTTTCTTAAAAAAATTAACACTTTAAAT  
CCAATAAGTAAATGTGGAAGGTTGGTGGAAATAGTTAGCTGGAACTCAGAATTGATATT  
AACTTTACCAAGCCTTTGTTACATTATTTTCTTCTACAATTTATGAATGAATAATCCT  
GCACTATCTATGCATTCAAACAATGATACATATGGTGCATATGTATATATGGCAAAAATC  
TAAGAAATGTAGCCAAATATTAATATTGCTTACACGTAAGTAGTCAAATCATGGTGGTTT  
TTTTTTATTTTCTTGATTTTGCAAGAAAATTAATAAAGAGGCTATTTACATTTTAAATGTA  
CAAATGTGTATACAAATATAATAGTTATGCTTTAAAAATCCAATAAATAAATGTAAGTAA  
AACATTTCTGAATTTTTTAAAGATTTCTCAATAGATCTAGGTATTCTTCTTAACCAAATA  
CTGATACTACCGTTAACCACTTCTGGAAAATTCTGGCAATTGGTCCCTTTGGGGAAGAAT  
TAGAGGAATCACTACTATACACACTTACTGTGGTATTCAAGTCCCTTCTCAAGGGGAAT  
TCGCCTATCTTTTTTTCTTAAGTAATATTTTATCTTTAATAGACAAATAATGGTTGTAT  
TTATTTACGGGATACAAAGTGACATTTTGATGCAAGCATACCTTGTGGAATGATCAAATC  
AGGCTAATTAACATATCTGTCTATCTCAAATGCTTATCCTTTCTTCAATTGTGGGAGCACTT  
AAAATCAATCTTTTAGCTATTTGGAAATATAAAATATATTTTCTAACTATATTTTAC  
TTACGATGTAGTGTAAATAGATCACAGAACCTATTTCTTCTATCTAACTGAACTTTGTGTA  
CTCTTTGACCAACATCTCCCCTTTCTTTGTCCATCCTCCTAGCCCAGCCTTTGGTAGCCA  
TCACTGTACTCTGTATTTCTATCACTTTGCCTTTTTAAATTGCACATATAAGAGAGATCA  
TGCAGTATTTGTTGCTTTGTGTCTGACTTATTTCCCTGTAGCAGAATGTCCTTTAGGTTAA  
TCCATGTTGTCTATAAATGACAAAATTTCCCTGCCTTTCAAAGGCTGAATAGTATTCATTG  
TTTATATATAACCAATTGTCAAATCCATTCACTCTGTTGATGGGCATGTAAGTTGTTTTTC  
AAATATTGGCTTTTATTAATAATGCGGCAGTGAACGTGGGAGTTTCAACATCTTTGTGACA  
TACTGATATTAATTCCTTTGACTATATACTCAAAAAGTGGAAATTGCTGGACTGTGTGGTAA  
TTTTAGATTTTTTAGTAACATTCATACTGTTTTCCAAAATAACTGTATGAATTAACAATAC  
CATCAACAATGTACAAGGGTTCCCTCTGCTCCACATCCTCATCAACACTTGCTAGTTTTTC  
ATGTTTTTCGATAATAGCCAGTCTATCAGGTGTAAGATAATATTTTCAATTGTGATTTAATTA  
GCATTTCTTTGATAATCAGAGATTTTGAGCCTTTTTTAATATATCTGTTGACCACTTTTA  
TGTTTTCTTTTGAGAAATGTGATTTTAAGTCTGCTGCCATTTTTTAATAGGATCAATTTGT  
TTTCTTATTATTGAGGGGTTTGAGTTCCATGCATATTTTAGATACTAGCCTTTTATCCAA  
TGCGTAATTTGCAAATATTTTCTCCCAATCTGTGGGTTGTCTCTTTAACCTGCTAACTGT  
TTCCTTTCCCTTCTGCAAGGCTTTTTAGTTTGATGCAATTCATTTGTCTATTTTTGTCT  
TCCATTGCCTGTGCTTTTGGGGTTAAGAAATCTCTGCTCGATTACATTTATTGATTTGCG  
TATATTGAACCAGCCTTGCCTCCACGGATGAAGCCCACTTGATCATGGTGGATAAGCTT  
TTTGATGTGCTGCTGGATTTCGTTTGCAGTATTTTATTGAGGATTTTTGCGTAGAGGTGT  
CATCAAGGATATTGGTCTAAAATCTCTCTTTTTGGTTGTGTCTCTGCCAGGCTTTGGTAT  
CAGGATGATGCTGGCCTCATAAAATGAGTTAGGGAGGATTCCCTCTTTTTCTATTGATTG  
GAATAGTTTCAGAAGGAATGGTACCATTCCCTCTGTACCTCTGGTAGAATTCGGCTGTG  
AATCCATCTGGTCTGGAATCTTTTTGGTTGGTAAACTATTGATTATTGCCACAATTTCA  
GAGCCTGTTATTGGTCTATTCAAGAGATTCAACTTCTTCTGTTTAGTCTTTGGGAGGGTG  
TATGTGTCAAGGAATTTATCCATTCTTCTAGATTTTCTAGTTTATTGCGTAGAGGTGT  
TTGTAGTATTCTCTGATGGTAGTTTGTATTTCTGTGGGATTGGTGGTGTATCCCTTTA  
TCATTTTTTATTGTGTCTATTTGATTCTTCTCTTTTTCTCTTTATTAGTCTTGCTAGC  
GGTCTATCAATTTTGTGATCCTTTCAAAAACCAGCTCCTGAATTCATCCATTTTTTTGA  
AGGGTTTTTTGTGTCTCTATTTCTTCTAGTTCTGCTCTGATTTTAGTTATTTCTTGCTT  
CTGCTAGCTTTTGAATGTGTTTGTCTTGTCTTTCTAGTTCTTTTAAATGTGATGTTAGG  
GTGTCAGTTTTGGATCTTTTCTGCTTTCTTGTGGGCATTTAGTGTATATAAATTTCCCT  
CTACACACTGCTTTGAATGTGTCCAGAGATTCTGGTATGTTGTGTCTTTTTTCTCGTTG  
GTTTCAAAGAACATCTTTATTTCTGCCTTCATTTGTTATGTACCCAGTAGTCATTTCAGG  
AGCAGGTTGTTCAAGTTTCCATGTAGTTGAGCAGTTTTGAGTGAGTTTCTTAATCCTGAGT  
TCTAGTTTGAATGCACCGTGGTCTGAGAGACAGTTTTGTATAATATCTGATCTTATACAT  
TTGCTGAGGAGAGCTTTACTTCCAATATGTGGTCAATTTTGAATAGGTGTGGTGTGGT  
GCTGAGAAGAAATGTATTTCTGTTGATTTTCCGGGTGGAGAGTTCTGTAGATGTCTATTAGG  
TCTGCTTGGTGCAGAGCTGAGTTCAATTCCTGGATATCCTTGTTAACTTTCTGTCTCGTT

FIG. 1AU

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GATCTGTCTTATGTTGACAGTGGGGTGTAAAGTCTCCCATTATTATTGTGTGGTAGTCT  
AAGTCTCTTTGTAGGTCACTCAGGACTTGCTTTATGAATCTGGGTGCTCCTATATTGGGT  
GCATATATATTTAGGATAGTTAGTCTCTTCTTGTTC AATTGATCCCTTTACCATTATGTAA  
TGGCCTTCTTTGTCTCTTTTGATCTTTGTTGGTTTAAAGTCTGTTTTATCAGAGACTAGG  
ATTGCAACCCCTGCCTTTTTTTGTTTTCCATTGCTTGGTAGATCTTCTCCATCCTTTT  
ACTTTGAGCCTATGTGTGTCTCTGCACGTGAGATGGGTCTCCTGAATACAGCACACTGAT  
GGGTCTTGACTCTTTATCCAATTTGCCAGTCTGTGTCTTTTAATTGGAGCATTTAGTCCC  
TTTACATTTAAAGTTAATATTGTTATGTGTGAATTTGATCCTGTCATTGTAATGTTAGCT  
GGTTATTTTGTGTTGTTAGTTGATGCAGTGTCTTCCCTAGCCTCTATGGTCTTTACAATTTG  
GCATGATTTTGCAGTGGCTGGTACTGGTTGTTCCCTTTCCATGTTTAGTGCTTCCCTCAGG  
AGCTCTTTTAGGGCAGGCCTAGTGGTGACAAAATTTCTCAGCATTTGCTTGTCTGTAAAG  
GATTTTATTTCTCCTTCACTTATGAAGCTTAGTTTGGCTGGATATGAAATCTGGGTTGA  
AAATCTTTTCTTTAAGAATGTTGAATATTGGCCCCACTCTCTTCTGACTTGTAGAGTT  
TCTGCCGAGAGATCCGCTGTTAGTCTGATGGGCTTCCCTTTGTGGGTAAACCCGACCTTTC  
TCTCTGGCTGCCCTTAACATTTTTTCCCTTCATTTCAACTTTGGTGAATCTGACAGTTATG  
TGTCTTGGAGTTGCTCTTCTCGAGGAGTATCTTTGTGGCATTCTCTGTATTTCTGAATC  
TGAATGTTGGCCTTCCCTGCTAGATTGGGGAAGTTCTCCTGGATAATATCCTGGAGAGTG  
TTTTCCAACCTTGCTTCCATTCTCCCCGTCACTTTCAGATACACCAATCAGACGTAGATTT  
GGTCTTTTACATAGTCCCATATTTCTTGGAGGCTTTGTCCGTTTCTTTTTATTCTTTTT  
TCTCTAAACTTCCCTTCTCACTTCACTTCACTTCACTTCACTTCACTTCACTTCACTTCACTT  
TCTTCCAGTTGATCGCATCGGCTCATGAGGCTTCTGCATTCTTACAGTAGTTCTCGAGCC  
TTGGCTTTCAGCTCCATCAGCTCCTTTAAGCACTTCTCTGTATTGGTTATTCTAGTTTTA  
CATTTGTCTAAATTTTTTTCAAAGTTTCAACTTCTTGCCTTTGGTTTGAATTTCTCC  
TGTAGCTCGGAGTAGTTTTATCGTCTGAAGCCTTCTTCTCTCAACTTGTCAAAGTCATTC  
TCCATTCACTTTGTTCCATTGCTGGTGAGGAGCTGCGTTTCCCTTTGGAGGAGGAGAGGTG  
CTCTGCTTTTTAGAGTTTCCAGTTTTCTGCTCTGTTTTTTCCCATCTTTGTGGTTTTA  
TCTACTTTTGGTCTTTGATGATGGTGATGTACAGATGGGGTTTTGGTGTGGATGCTCTTC  
CTGTTTGTAGTTTTTCTTCTAATAGACAGGACCCTCAGCTGCAGGTCTGTTGGAGTTTG  
CTAGAGGTCCACTCCAGACCCTGTTTGCCTGGGTACCAGCAGCGGTGGCTGCAGAAGAGC  
GGATTTTCGTGAACCGCAATGCTGCTGTCTGATCGTTCCCTCTGGAAGTTTTGTCTCAGA  
GGAGTATCCTGCCGTGTGATGTGTGAGTGTGCCCCCTACTGGGGGGTGCCTCCAGTTAGG  
CAGATGACATGGTTGTATATCTAGAAAGCCCCATTATCTCAGTCCAAAATCTCCTTAAGC  
TCCAGCTGCGTGTCTGGGAGAACCCTGCTCTCTTCAAAGCTGTGCGACAGGGACATTTAA  
GTCTGCAGAGGTTACTGCTGTCTTTTTGTTTGTCTGTGCCCTGCCCCAGAGGTAGAGCC  
CACAGAGGCAGGCAGGCCTCCTTGAGCTGTGGTGGGCTCCACCCAGTTCGAGCTTCATGG  
CTGCTTTGTTTACCTAAGCAAGTTTGGGCAATGGCGGGCACCTCTCCCCAGCCTTGCTG  
CCACCTTGCAGTTTGTATCTCAGACTGCTGTGCTAGCAATCAGCAAGACTCTGTGGGCATA  
GGCCTTCCAGCATATAAACAGAACCAAGACAAAACCATATGATTATCTCAATAAATTAG  
CAGAAAGGGCCTTTGACAAGATTCAACAACGCTTCATGCTAAAAACTCTCAATAAATTAG  
GTATTGATGGGATGTATCTCAAAATAATAACAGCTACTTATGACAAACCCACAGCCAACA  
TCATACTGAATAGGCAAAACCTGGAAGCATTCCTTTTGGAACTGGCACAAGACAGGGAT  
GCCCTCTCTCACCCTCCTATTCAACATAGTGTTGGAAGTTCTGGCCAGGCAATTAGGC  
AGGAGAAGGAAATAAAGGGTATTTCGATTAGGAAAAGAGGAAGTCAAATTGTCCCTGTTTG  
CAGATGACATGGTTGTATATCTAGAAAGCCCCATTATCTCAGTCCAAAATCTCCTTAAGC  
TGATAAGCAACTTCAGCAAAGTCTCAGGATACAAAATCAATGTACAAAATCACAAGAAT  
TATTACACACCAATAACAGACAAATAGAGAGCCAAATCATGAGTGAATCTCATTACAA  
TTGCTTCAAAGAGAATAAAATACCTAGGAATCCAACCTTACAAGGGACGTGAAGGACCTCT  
TCAAGGGAACTACAAACCACTGCTCAATGAAATAAAAGAGGATACAAACAAATGGAAGA  
ACATTTCCATGCTCATGGTTAGGAAGAATCAATATCGTGAAAATGGTCATACTGCCCAATG  
TAATTTATATATTCAATGCCATCCCCATCAAGCTACCAATGACTTTCTTACAGAATTGG  
AAAAAACTACTTTAAAGTTTCAATATGGCACCAAAAAAGAGCCCGCATCACCAGTCAATCC  
TAAGCCAAAAGAACAAGCTGGAGGCATCACACTACCTGACTTCAAATATACTACAAGG  
CTACAGTAACCAAAACAGCATGGTACTGGTACCAAAACAGAGATATAGCTCAATGGAACA  
GAACAGAGCCCTCAGAAATAATGCTGCATATCTACAATATCTGATCTTTGACAAACCTG  
AGAAAAACAAGCAATGGGGAAAGGATTCCCTATTTAATAAATGGTGTGGGAAAACCTGGT  
TAGCTATATGTAGAAAGCTGAAACTGGATCCCTTCCCTTACAGCTTATTCTAAAATTAAC  
CAAGATGGATTAAAGACTTAAACGTTAGACCTAAACCATAAAAACCTAGAAGAAAACCT

FIG. 1AV

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AGGCATTACCATTCAGGACATAGACATGTGCAAGGACTTCATGTCTAAAGCACCAAAAGC  
AATGGCAACAAAAGCCAAAATTGACAAATGGGATCTAATTAAACTAAAGAGCTTCTGCAC  
AGCCAAAGAACTACCATCAGAGTGAGCAGGCAACCTACAAAGTGGGAGAAAATTTTCGC  
AACCTACTTATCTGACAAAGGGCTAATATCCAGAATCTACAATGAACTAAAGCAAATTTA  
CAAGAAAAAACAAACAACCCCATCAAAAAGTGGGTGAAGGATATAAACAGACACTTCTC  
AAAAGAAGACATTTGTGCGACCAAAAAACACATGAAAAAATGCTCATCATCACTGGCCAT  
CAGAGAAATGCAAATCAAACCACAATAAGATACCATCTCACACCACTTAGAATGGCAAT  
CATTAAAAAGTCAGGAAACAACAGGTGCTGGAGAAGATGTGGAGAAATAGAAACACTTTT  
ACACTGTTGGTGGGACTGTAACTAGTTCAACCATTGTGGAAGTCAGTGTGGCGATTTCCT  
CAGGGATCTAGAACTAGAAATACCATTTGACCCAGCCATCCCATTACTGGGTATATACCC  
AAAGGACTATAAATCATGCTGCTATAAAGACACATGCACACGTATGTTTATTGTGGCACT  
ATTACAAATAGCAAAGACTTGGAACCAACCCAAATGTCCAACAATGATAGACTGGATTAA  
GAAAATGTGGCACATATACACCATGGAATATGTCAGCCATAAAAAAGGATGAGTTCAT  
GTCCTTTGTAGGGACATGGATGAAATTGGAAATCATCATTCTCAGTAACTATTGTAAGA  
ACAAAAAACCAACACCGCATATGCTCACTCATAGGTGGGAATTGAACAATGAGAACACA  
TGGACACAGGAAGGGGAACATCACACTCTGGGGACTGTTGGGTGGGGGGAGGGGGAGGG  
ATAGCCTTAGGAAATATACCTAATTATAAATGACGAGTTAATGGGTGCAGCACAGCGCA  
TGGCACATGTATGCATATGTAACCTGCACATTGTGCACATGTACCCTAAAACTTAA  
AGTATAATAATAAAAAATAAAAAATAAAGAATAGAATAAATAAAAAACAAAAATAATA  
AAAAATAAAAAAGAAATCTCTGCTCATATCCAGGCCATGATGGTTTTCCCCCTGTGTTTTCT  
TCAAGTAGTTTTATAGCTTCAAGTCTTATGTTATATTAAGTCTTTAATCCATTTTGAGGT  
GATTCTTGTACAAAGGCTGAAGTAAGGGTTCATTTTGATTCTTCTGTGTGTGTGTATCCA  
GTTTTCCCAACACCATTTATTGAGAAGTCTGTCATTTCCCATGGTGTGATCTTGTACC  
TTTATGAAAAATTAATTGACCATAGGTGTATGGGTTTTATTTCTGGGCTTTCTATCATATT  
CCATTGATTGATATGTCTGGTTTTATGCCAGTACTATGCTGCTTTGATTACTGTGGATTT  
GTAATGTAATTTAATGTCTGAGAGTGTGAAGCCTGCAGCATTATTTTTCTCAAGATTGT  
TATCTGTGGCTATTTGTAGTCTTTTGTGGTTTCATATATATTTTACAATTTTTTATTTCT  
GTGAAAAATGCATTGGAATTTTCATATGGATTACATTTAATCCGCTTTGGGTAGTATGAC  
CATTTTAACAATATTAATTGTTCTAATCCATGAGCATGGGCTAGCTTTTTCATTTATTTGT  
GTCATCTTCAGGTTTTTTCAACAATGTTTTATAGTTTTAGTATATGGATCTTTCACTTCC  
TTGGTTAAATTTAGTCCCTAAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT  
GTGTGTGTGCATCAACTAACCATAGTCATGTGGGTTTTATTTCTGGGCTTTCTATCATGTT  
CCATTGATTACTTCTAAGTGAATGAGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT  
ACTGTTGTAATTTTAAATTTCTTTCTCAGGTTGTATGTTGTTAGTGTACAGAAATAATA  
TTAATTTTGTAGTTGATTTTGTATTTCTGCAAATTCACATAAATTTGTTAATTTGTTTTAA  
CAATTTTTTGGGTGTAGTCTTACAGGGTTTTCTATATATAAGATCATGTCATCAGTAAAC  
AATTTTCATTTATTCTTTTCCATTTTGGATGCTTTTTATTCTTACCCAATTGTTTTGACTA  
GGACCTCCAGTACTATGTTGAACATAATTGATGAAAGCAGACATCCTTGTCTTGCTCCTG  
ATCCAAAAGCCTTTAACTTTTCACCACTGAGTATGATGTTCACTGTAGGCTTGTATATA  
TGGTCTTTGTGTGCTGAGAAACATTCCTTCTATAACTGATTTTCAAAGTTTATCATGA  
AAGGATGTTAAATATTTCAAATGTTTTTCTTCATCTATTGAGGTGATTATATTGTTTT  
TATTCTTCATTTCTGTTACTATGGTGAATCATATTTTAAATGTTTTTACTTGCATAAAT  
TTATTTTGTGATAGGTAGAAAAGCACATCTGCAGACCTAGAAGCAGAGTGAATCTAAAAA  
ATATTATTTATAATTATTATGAGTACACAATAGGTATATATTTTCATGGGGTACATTCAA  
TGTTCTGATACAGGCATATGATGTGTAATAATCACATCAGGGTATTTGGAGTATTCATTA  
CCTCAAGCATTTATCATTTCTTTGTGTTAGGGAATTTCAAGTTTCATTCTTCTAGTTATTT  
AAAATATACAATGAATTATTATTGACTGTAGTCACCCCTGTTGTGCTATCAAATAGTATGT  
CTTATTTCATTTTATTTAACTATATTTTGCACCCATTAAACAATCCCCACTTGATTTGAAT  
ATGGTAAGCCATTCTTGCATCCTAGGAATAAATTCATTTGACCATGGTGAATGATCCTT  
TTAATGTACTGTTGAATATAGTTTTTGGTATTTTGTGAGGATTTTGCATCCATGTTCA  
TCAGCGATATTGGCCTGTAATTTGCTTTTCCGGTAGTTTCTTGTTTTTTTATTATACTTT  
AAGTTTTAGGGTACATGTGCACAACGTGCAGGTAGTTACATATATATACATGTGCCATA  
TTGGTGTGCTGCACCCATTAACTCATCATTTAACATTATGGAAAAATCTCCTAATGCTATC  
CTCCCCGCTCCCCCACCACAGGCCCCGGTGTGTGATGTTTCGCTTCTGTGTCT  
CATGTGTTCTCATTTGTTCAATTCCACCTATGAGTGAACACACAGGTGTTTCTTAGTCT  
GGCTTTGGTCTCAGGCTAATGTTGGCCTTACAAAATGATTGTGGAAATATTTCTTCTCT  
TCAATTTTTTGAAGAAGTTTGAAAATAATTATTACCAGTTCTTCTATAAATGTTGGGTAG

FIG. 1AW



FIG. 1AX



[illegible]

FIG. 1AY